The New England
Journal of Medicine

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Volume 254 MAY 3, 1956 Number 18

SYMPOSIUM ON THE DIAGNOSIS AND TREATMENT OF MITRAL-VALVE DISEASE*

INTRODUCTION

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BOSTON

THE Eastern Conference of Radiologists was held in Boston on March 3, 4 and 5, 1955. The meetings of this group have been held in rotation in New York, Philadelphia, Baltimore, Washington and Boston for the past thirty years. The scientific program of each meeting is presented entirely by members of the host society, and by custom is expected to be a cross-section of the original or investigative work being done in the field of radiology or its allied areas. Because of the extreme importance of accurate preoperative investigation of patients being considered for surgery of acquired mitral-valve lesions and in view of the advanced work being done by Boston physicians and surgeons in this field, a symposium on the diagnosis and treatment of mitral-valve disease was arranged and presented on March 5, 1955. The four papers immediately following this introduction stimulated a great deal of discussion (which unfortunately was not adequately recorded) and are presented herewith in response to many requests for publication.

*Held in Boston, March 5, 1955.
†Chairman of the Symposium.

MITRAL-VALVE DISEASE‡

A Radiologic Approach to a Physiologic Diagnosis

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BOSTON

WITH the advent of commissurotomy and valvuloplasty for the surgical correction of mitral stenosis, it became of more than academic interest to differentiate the two components of combined mitral-valve disease. Early attempts to do this were frustrated by the paucity of data against which the accuracy of radiologic impressions could be checked, especially in patients who defied classification by any technic as having stenosis or insufficiency as their incapacitating lesion.

Many patients, subsequently shown to have widely different valve sizes, presented confusing and overlapping x-ray changes (Fig. 1.). As a result, the validity of x-ray opinion was limited largely to the ends of the spectrum where the two entities exist separately in what might be termed classic form (Fig. 2).

In an attempt to define the problem, the x-ray studies on 100 patients were critically analyzed for purposes of standardizing the evaluation of the specific features of mitral-valve disease. When the data from cardiac catheterization and operative procedures became available, these cases were again reviewed, as unknowns, in terms of both individual features and diagnosis. The 43 patients on whom the most complete and reliable catheter and operative data were accumulated form the principal basis of this report.

From the outset, interest has been focused on patients in whom the two entities of mitral stenosis and insufficiency merge, but not for the purpose of identifying the superimposition of the two defects. Rather, it has been the hope, on the assumption that the two defects do not exist together functionally in

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severe form, to evolve criteria whereby the x-ray examination can help identify the physiologically predominant lesion. Only in this way can the simple x-ray studies assume a significant role in the screening of patients for operative selection.

Radiographic Features

Features of the x-ray examination that have not been critical in this objective are listed in the left-hand column of Table 1. Any one of these features may be of definite diagnostic aid in a given case. A small or only slightly enlarged heart may occur in severe mitral stenosis but is rarely, if ever, present with incapacitating insufficiency. Nodular, fibrotic hemosiderosis of the lungs accompanies stenosis rather than regurgitation. In certain cases, a grossly elevated or depressed cardiac apex provides reliable evidence of ventricular preponderance. However, in the material under consideration, examples of this sort have been infrequent.

The evidence exists that expansile pulsation does, in reality, reflect changes in atrial volume in the presence of significant regurgitant flow. On the other hand, the competent observation of systolic expansion in patients with small mitral-valve orifices casts some doubt on whether the motion seen at fluoroscopy and on the kymogram always reflects volume change, especially considering the left-atrium pressure-volume relations that result from these stenotic valves. Efforts to evaluate it as a function of total volume change in the atrium on the basis of both forward and backward flow have been unrewarding to date. These facts, combined with the fact that one often cannot detect systolic expansion in the huge atria of advanced mitral regurgitation, make it, at present, a finding of uncertain diagnostic help in the classification sought.

Similarly, calcification in the mitral valve implies organic stenosis and, indeed, one hesitates to make the diagnosis without its detection when the differential choice resides between mitral stenosis and some other defect that simulates it physiologically. Alternatively, its identification by x-ray study has an anatomic rather than physiologic connotation when one is dealing with combined rheumatic valvular disease. It may be that massively calcified valves are uncommon in free regurgitation, but estimates of size and distribution of calcium, to say nothing of its presence or absence on x-ray study, have not helped distinguish the important physiologic deficit in the average case.

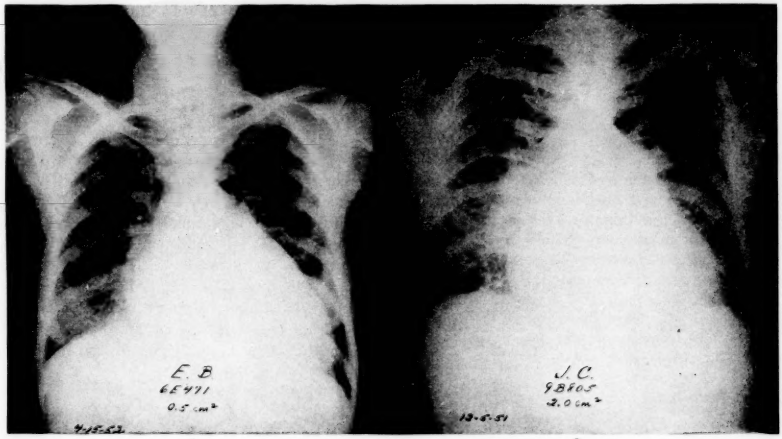

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Figure 1. *Roentgenograms, Showing Tight Mitral Stenosis, Valve Size of 0.5 Sq. Cm. (Left) and Predominant Mitral Regurgitation, Valve Size of 2.0 Sq. Cm. (Right).*

The radiographic features that have been helpful are listed in the right-hand column of Table 1. Of perhaps greater significance than the size per se is the contour of the left atrium as it projects posteriorly and impinges on the barium-filled esophagus. Although in part an indication of total atrial size or volume, it also reflects the size of the left ventricle and the level and turgidity of the left atrium — and therefore merits specific evaluation as an entity.

This configuration may be classified as either interrupted or continuous, depending on whether the posterior bulge "breaks" above the level of the diaphragm — resulting in a localized bulge — or whether there is a sweeping, continuous curve (Fig. 3). The distinction may be made in either the oblique or lateral projections, although it can frequently be de-

fined in the lateral view when it is not obvious in the other two.

Because of difficulties in evaluating slight degrees of enlargement of one ventricle in the presence of more marked enlargement of the other, especially when the left is the less enlarged of the two, the concept of ventricular dominance has been adopted (Table 1). Accordingly, ventricular size is interpreted in terms of whether the configuration is fairly unequivocally dominant right, unequivocally dominant left or questionably dominant in either direction.

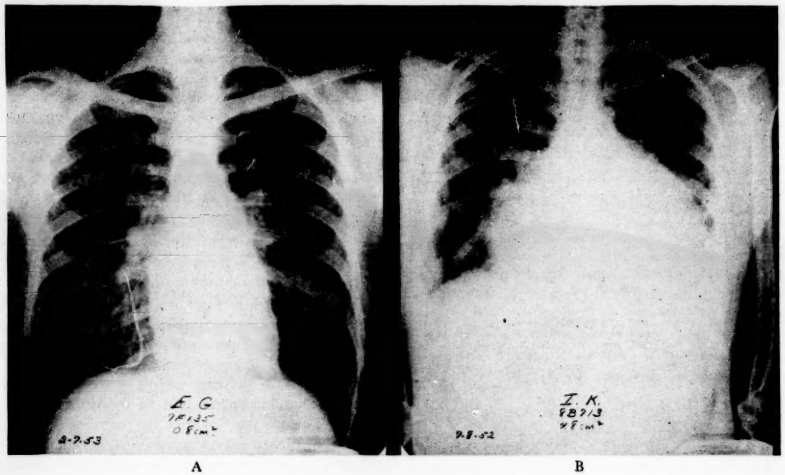

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FIGURE 2. *Roentgenograms, Showing "Classic" Mitral Stenosis, Valve Size of 0.8 Sq. Cm. (Left) and Advanced Mitral Incompetence, Valve Size of 4.8 Sq. Cm. (Right).*

TABLE 1. *Evaluation of Radiologic Criteria for the Analysis of Mitral-Valve Disease.*

INCONSISTENTLY HELPFUL CRITERIA	CONSISTENTLY HELPFUL CRITERIA
Heart size	Size of main pulmonary artery
Appearance of pulmonary vasculature	Size of left atrium
Level of cardiac apex	Contour of left atrium
Expansile pulsation of left atrium	Ventricular dominance
Valvular calcification	Size of aorta

Finally, an attempt is made to evaluate the size of the aorta in the light of the patient's age and the presence or absence of complicating cardiovascular defects. Although such an evaluation is only an impression, it is usually not difficult to recognize the definitely small or hypoplastic aortas.

The trends that the helpful criteria follow as one proceeds along the spectrum from very tight mitral stenosis to free mitral regurgitation are detailed in the "Mahatma formula" of mitral-valve disease (Table 2). The values are arbitrary and in themselves meaningless. The first two — size of pulmonary artery and left atrium — represent numerical values assigned for purposes of illustrating trends. The figures for the second two, the interrupted atrial contour and hypoplastic aorta, reflect the incidence of these findings expressed as a ratio to the number of observations. Correspondingly, the values for ventricular dominance indicate the incidence of dominance of the right ventricle expressed as a ratio to the number of patients. The headings of the three columns represent three classifications of valve size, ranging from the

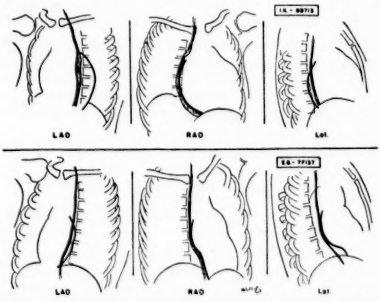

FIGURE 3. *Diagrams, Showing Sweeping, Continuous Contour of the Left Atrium in Predominant Mitral Insufficiency (Upper Section) and "High" Atrial Impression, with the Interrupted Contour of Mitral Stenosis (Lower Section).*

tiny valves of mitral stenosis to the large valves of mitral incompetence.

TABLE 2. *Mahatma Formula for Evaluation of Mitral-Valve Disease.*

CLASSIFICATION	VALVE SIZE OF 0.2-1.0 SQ. CM.	VALVE SIZE OF 1.1-1.9 SQ. CM.	VALVE SIZE OF 2.0 SQ. CM. & OVER
PA*	4.0	2.8	2.8
LA†	3.3	4.3	5.6
I/C‡	0.8	0.7	0.5
A§	0.6	0.4	0.8
VD¶	0.8	0.7	0

*Size of main-pulmonary-artery segment in 2 views, divided by no. of patients.
†Size of left atrium in 2 views, divided by no. of patients.
‡Ratio of interrupted contour to no. of patients.
§Ratio of hypoplastic aortas to no. of patients.
¶Ratio of those with unequivocal dominance of right ventricle to no. of patients.

For this table it can be seen that, as one progresses from frank mitral stenosis to free regurgitation, pulmonary-artery size changes in inverse relation to left-atrium size, the interrupted atrial contour becomes an increasingly less prominent feature, dominance of the right ventricle gives way to left, and the aorta tends to be more hypoplastic at the extremes of the spectrum and more normal in the intermediate ranges.

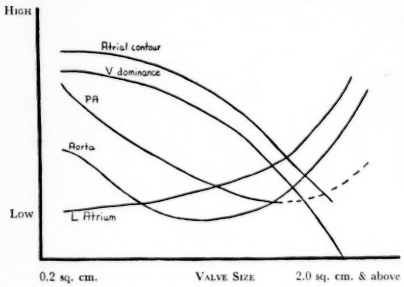

FIGURE 4. *"Mahatma Formula" of Mitral-Valve Disease, Depicted Graphically.*

Figure 4 presents these trends schematically in graphic form. The numerical values, extending from the low to high ranges, are plotted on the ordinate; the values along the abscissa indicate mitral-valve size expressed in square centimeters of the surface area.

The incidence of the right-ventricle dominant configuration is depicted as decreasing to the point where it does not exist in patients with advanced and marked regurgitation. Thus, as one proceeds along the spectrum, the enlarging left ventricle finally achieves frank domination. As this takes place and as the left atrium enlarges, the incidence of the interrupted contour declines in favor of the continuous configuration.

The dotted extension of the main-pulmonary-artery-size curve is indicated to convey the thought that one might expect it to rise again in patients with patulous valves, if they were able to survive such severe degrees of mitral insufficiency.

In the past, little attention has been paid to the aorta, but the catenary shape of the aortic curve gives it the potential at least to hold a key to the diagnosis. If the aorta is definitely hypoplastic, the chances of its being toward the ends of the spectrum are great, and the diagnosis should not be too difficult. If, on the other hand, the aorta is fairly normal in size, the chances of its being at the middle portion of the curve are greater, and the radiologist can orient himself on the abscissa, depending on the other findings.

The background considerations for the practical application of these criteria are presented in Table 3, which indicates the physiologic classifications into which patients with various valve sizes will fall. Again, valve sizes are reported in square centimeters of surface area.

Adding to this table the accuracy of the x-ray examinations, reviewed as unknowns and appraised in terms of catheterization and operative data, one defines the correlations with abnormal physiology. The figure at the left (0.906) reflects the ratio of patients with roentgenologically predominant mitral stenosis who did, in fact, fall into the indicated classification

TABLE 3. *Accuracy of the Roentgenographic Method in Relation to Abnormal Mitral-Valve Physiology.*

← VALVE SIZE OF —— 1.2 SQ. CM.	VALVE SIZE OF 1.2 —— 1.3 SQ. CM.	VALVE SIZE OF 1.4 —— 1.6 SQ. CM.	VALVE SIZE OF 1.7 —— 1.8 SQ. CM.	VALVE SIZE OF 1.8 —— → SQ. CM.
Surely mitral stenosis	Very probably mitral stenosis	Hard to tell One leans toward mitral incompetence (Valvuloplasty may be helpful in this group especially if cardiac output up)	Very probably mitral incompetence	Surely mitral incompetence
		BATTING AVERAGE		
← 0.906		0.500		0.833 →

GRAND AVERAGES: 0.857 correct valve size
0.895 correct physiologic classification

of valve size, expressed as a batting average or the number of "hits" per time at bat. Similarly, the figure on the right (0.833) reflects the ratio of patients with roentgenologically predominant mitral incompetence who fell into the designated orifice ranges. The central figure (0.500) indicates the ratio of patients with an inconclusive roentgenologic impression who fell into the borderline valve range (only 2 out of 4 patients).

If one combines all the averages, one achieves a fairly high accuracy (0.857) in being able to group patients in the correct valve-size range. By combining the averages at the outer ends of the spectrum so as to include only those patients about whom a confident opinion could be expressed (39 out of 43 patients), one derives a consoling average (0.895) in being able to place patients in the correct physiologic classification.

Discussion

Forty-three patients comprise too small a group to be of statistical value. That the formula can be of definite assistance, however, is evidenced by the fact that the same order of accuracy has been achieved in the entire series of 100 patients. In 57 of these, the exact valve size has been less comprehensively documented, but correlation with clinical and operative data has been a reliable basis for evaluating the correct physiologic category. Since about two thirds of these patients have had fairly definite physiologic mitral stenosis and about a quarter have had fairly definite physiologic mitral incompetence, it has been possible to fulfill the objective of predicting the proper physiologic classification in 90 per cent of cases — reassurance that an x-ray opinion of confidence can carry a conviction of fact. This level of accuracy is abetted by the fact that only about 10 per cent of the material has fallen into the borderline physiologic range.

Of equal significance has been the recognition of the radiologic "penumbral" area as an indicator for additional and more elaborate diagnostic effort, up to and including exploratory cardiotomy, in patients whose physiologic status cannot be decided on clinical grounds.

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PHYSIOLOGIC CHANGES IN MITRAL STENOSIS*

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BOSTON

THE effects of mitral stenosis on the heart and lungs are due to an obstructive lesion between the left atrium and ventricle. The bodily response to such an obstruction is initially twofold. Most important is a rise of pressure proximal to the obstruction — that is, in the left atrium, pulmonary veins, pulmonary capillaries, pulmonary artery and right ventricle. The amount of blood passing through the obstructed area — the cardiac output — becomes reduced.

The size of the orifice of the normal mitral valve in an adult is about 5 sq. cm. The pressure in the left atrium is normally about 5 mm. of mercury. The normal cardiac output is about 5.5 or 6.0 liters per minute. As the mitral valve becomes narrow over an average period of perhaps twenty-five to thirty years, as a result of rheumatic fever, the size of its orifice diminishes. Critical narrowing can be said to occur when the orifice is at or about 1.0 sq. cm. (This is critical narrowing in the sense that all patients are then thoroughly symptomatic.) The pressure in the left atrium at rest has gradually risen as the orifice of the valve has narrowed until at a size of 1.0 sq. cm. the usual value for pressure is at or near 25 mm. of mercury and the cardiac output has fallen in the average case to 4.0 or 4.5 liters per minute.

Any rise of pressure in the left atrium, of course, is accompanied by a similar rise of pressure in the lungs and right ventricle. The *locus minoris resistentiae* of this circuit is the pulmonary capillaries. Any rise of pressure above the osmotic pressure of plasma

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(25 mm. of mercury) results in a transudation of fluid from capillaries to alveoli. Thus, at a valve size of 1.0 sq. cm. with a pressure in the left atrium, and therefore in the pulmonary capillaries, at or about 25 mm. of mercury, the patient becomes almost bed ridden because mild activity or emotion produces a rise of pressure in the pulmonary capillaries above the osmotic pressure of plasma, a transudation of fluid from capillaries to alveoli and microscopical or gross pulmonary edema. It is for this reason that dyspnea is the most prominent feature.

One of the earliest manifestations of mitral stenosis is radiologic enlargement of the left atrium, reflecting the increase of pressure within that chamber. Indeed, the enlargement frequently precedes the apical diastolic murmur. Not until the valve orifice approaches 1.0 sq. cm. do the pulmonary vascular markings become prominent and radiologic evidences of pulmonary edema appear. This initial bodily response to mitral-valve obstruction is *not* accompanied by enlargement of the pulmonary artery, of the right ventricle or of the heart as a whole. Enlargement of these structures does not occur as a result of mitral stenosis alone but only as a consequence of mitral stenosis combined with changes in the pulmonary blood vessels. The syndrome described to this point is one of mitral stenosis of varying degree, culminating in a valve size of about 1.0 sq. cm., at which point respiratory distress may be devastating and yet, except for the left atrium and pulmonary vascular markings, the heart is of perfectly normal size.

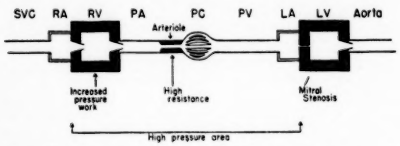

FIGURE 1. *Diagram of the Central Circulation, Showing the Pathologic Physiology of Mitral Stenosis.*

In the vast majority of patients, it is at this point (but not earlier), when pulmonary edema impends as a chronic state, that pulmonary vascular changes appear. These vascular lesions produce an obstruction to blood flow through the lung. The normal lung offers little resistance to blood flow. Large volumes of blood pass through the pulmonary vasculature at low pressures. In severe mitral stenosis, however, the resistance offered by the pulmonary vasculature increases as a result of structural changes in the arterioles and small arteries and also of vasoconstriction (Fig. 1). Thus, two stenoses are present in the lesser circuit — one at the mitral valve, and one in the lung. The stenosis in the lung has all degrees of mildness and severity. In the most severe form, the pulmonary vascular resistance may increase twenty-fold and may actually offer a greater barrier to blood flow than the mitral stenosis itself.

The effect of this pulmonary vascular obstruction is again twofold: pressure proximal to it in the pulmonary artery and right ventricle rises; blood flow, or cardiac output, falls even farther — in the most advanced cases to as little as 3 liters per minute. The decline of output allows the mitral valve to become smaller, as little as 0.3 sq. cm., the pressure in the left atrium remaining at or near 25 mm. of mercury. With the two resistances in series, pressure in the pulmonary artery must rise inordinately to force blood through to the left side of the heart. In the most severe cases, pressure in the pulmonary artery, which is normally 25 systolic, 9 diastolic, may exceed the arterial pressure in the systemic circuit. Pressures as high as 140 systolic, 75 diastolic, have been recorded in the pulmonary artery. It is the right ventricle, of course, that must pump blood at this pressure in the pulmonary artery. In so doing, it becomes hypertrophied and eventually dilates and fails. It is only with the advent of pulmonary vascular disease superimposed on the mitral stenosis that the right ventricle and pulmonary artery become enlarged, and in severe cases they may become huge, depending on the severity of the pulmonary vascular process. It is only then that the transverse diameter of the heart becomes abnormal. It is to be noted that the left ventricle and aorta do not partake in this enlargement. Indeed, because the cardiac output is reduced, they become smaller than normal and appear hypoplastic. In some cases, the left ventricle may appear slightly prominent, owing, undoubtedly, to displacement by enlargement of structures on the right side of the heart.

At surgery, mitral stenosis can be relieved readily but there is no direct surgical approach to relief of the pulmonary vascular obstruction. Present evidence is convincing, however, that relief of mitral stenosis is followed over the course of six months to a year by the gradual return of the pulmonary vascular resistance to normal. This is indeed fortuitous, for if the high pulmonary vascular resistance persisted, the patient would remain incapacitated.

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LATE FOLLOW-UP STUDY OF RADIOLOGIC CHANGES AFTER MITRAL VALVULOPLASTY

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AN objective radiologic survey of all patients who had undergone mitral valvuloplasty at the Mount Auburn hospital before January, 1954, was carried out. All patients in this group were operated upon by Dr. Dwight E. Harken. They were all studied both before operation and at follow-up examination by the cardiologists, Dr. Laurence B. Ellis and his associates, Drs. Walter H. Abelmann, John F. Otto, Jr., and J. Morrison Hutcheson, Jr. The clinical, electrocardiographic and laboratory findings will be reported elsewhere.

TABLE 1. *History of Symptoms As Given by the Patient at the Time of Fluoroscopy before Operation and at the Time of Fluoroscopy during Follow-up Examination Twelve to Thirty Months after Operation.*

SYMPTOM	BEFORE OPERATION	AFTER OPERATION
	NO. OF PATIENTS	NO. OF PATIENTS
Dyspnea*	54	10
Fatigue	50	17
Cough	45	17
Paroxysmal nocturnal dyspnea	43	2
Orthopnea	40	8
Hemoptysis	32	2
Dependent edema	28	8
Pulmonary edema	27	0
Exertional chest pain	24	11
Palpitation	21	2
Peripheral emboli	7	1

*On climbing 1 flight of stairs.

TABLE 2. *Abnormalities Seen at the Time of Radiologic Examination before Operation and at Follow-up Examination Twelve to Thirty Months after Operation.*

ABNORMALITY	BEFORE OPERATION	AFTER OPERATION
	NO. OF PATIENTS	NO. OF PATIENTS
Enlargement of left atrium	55	55
Displacement of esophagus	55	55
Enlargement of peripheral pulmonary vessels	50	40
Enlargement of main pulmonary artery	49	45
Enlargement of right ventricle	42	38
Visible left atrium in posteroanterior film	37	32
Calcified mitral valve	16	18
Mitral regurgitation	7	7
Enlargement of left ventricle	4	5
Pleural effusion	1*	1†

*Right sided.
†Left sided.

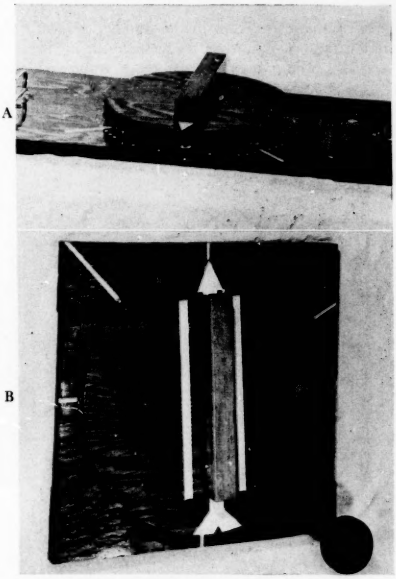

FIGURE 1. *Turntables Used during Fluoroscopy* (A) *and Radiography* (B) *That Make It Possible to Obtain Oblique Films at the Desired Angle and to Reproduce the Same Angles at Any Later Date.*

Turntable A, which is used during fluoroscopy, is placed on the regular foot board found on all standard fluoroscopic tilt tables. The patient stands with one foot flush against each side of the bar on the top surface of the device. When the brake pedal (at right) is depressed, the table is free to rotate, and the patient can be turned at will to the projection that shows the abnormalities of the heart to best advantage. A luminous arrow and degree markers enable the physician to order oblique films that duplicate what was seen at fluoroscopy.

Turntable B, which is used in the radiography room, enables the technician to reproduce oblique views as directed. The angles used are recorded in the patient's record so that identical projections can be reproduced at any later date. The device can, of course, also be used for other radiologic problems.

Only two criteria for selection were used: the patient had to be at least one year beyond operation and to live within 200 miles of Boston (the latter was

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stipulated because the patients paid their own expenses). Fifty-six patients were eligible, and 55 of them returned. There were 47 women and 8 men in the group, and the ages ranged from seventeen to fifty-three years.

The interval between operation and follow-up examination ranged from twelve to thirty months, with an average of about nineteen months.

Changes in Signs and Symptoms

A dramatic decrease in the number of symptoms at the time of follow-up study is shown in Table 1. Actually, the patients were more improved than Table 1 indicates since it only presents complete relief from any given symptom. Decreases in severity of symptoms were almost the rule even though some degree of disability persisted.

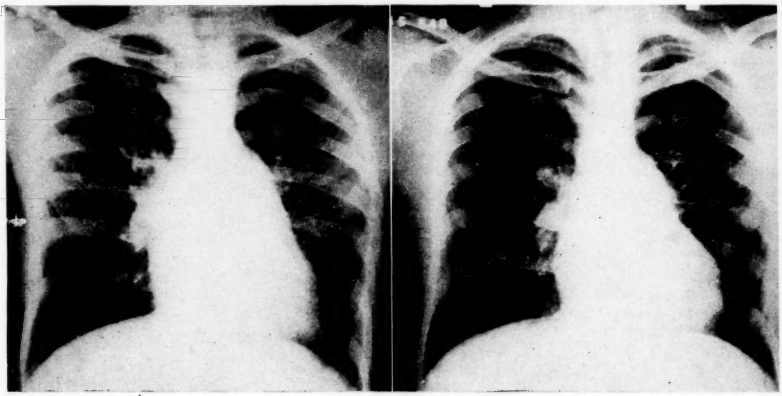

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FIGURE 2. *Films in Patient A.T.*

A preoperative film, taken on August 4, 1953 (A), *shows marked enlargement of the main pulmonary artery and moderate engorgement of the peripheral pulmonary vessels. Measurements: transverse diameter, 13.0 cm.; long diameter, 15.0 cm.; broad diameter, 11.3 cm. No intracardiac calcification was seen.*

A follow-up film taken on November 15, 1954 (B), *shows a decrease in the size of the main pulmonary artery and a slight decrease in the amount of engorgement of the peripheral pulmonary vessels. Measurements: transverse diameter, 12.3 cm.; long diameter, 13.8 cm.; broad diameter, 10.8 cm.*

Radiologic Abnormalities

One commonly used index of heart size, its transverse diameter, is of little value in mitral-valve disease, since most of the enlargement is not transversely, but rather in the anteroposterior direction. Only 5 of the 55 patients had a decrease in transverse diameter of more than 1 cm. Six showed an increase in transverse diameter of more than 1 cm.

Changes in the size of individual heart chambers and of the pulmonary vessels are more important (Table 2). Like the symptoms, the changes were more impressive than this table indicates, since a decrease in size of any structure is not listed unless the change was a complete return to normal.

In over half the patients the enlarged left atrium was visible in the posteroanterior film of the chest, either as a separate curve on the right border of the heart or as a definite extra density at the base of the heart.

A calcified mitral valve was found 16 times preoperatively. All these, as well as 4 others, were calcified as judged by the surgeon at operation. Two of the 4 that were not seen at fluoroscopy before operation were detected at the follow-up examination. In no case did a valve become visibly calcified in the interval between operation and the follow-up examination. *It is fair to say that if the valve is calcified enough for the surgeon to feel it, it should be seen at fluoroscopy.*

Regurgitation is another matter. It was thought to be present, in addition to stenosis, in 7 cases as judged by apparent systolic expansion of the left atrium. Only 2 of these were verified at operation, and in 7 other cases a regurgitant jet was felt by the surgeon at operation when regurgitation had not been suspected at fluoroscopy. In short, the radiologist agreed with the surgeon only twice. Fortunately, in this study the patients who did show regurgitation at operation also had a stenosis that could be relieved. At follow-up study it was found that this group fared almost as well as those with pure ste-

nosis. This is evidence that stenosis was the dominant lesion.

Oblique views have been a disappointment when heart size before and after operation is compared, owing to the difficulty in obtaining films made in exactly the same degree of obliquity. A turntable, or protractor, constructed to overcome this problem should make the oblique views more useful in future follow-up studies (Fig. 1).

Illustrative Case Reports

T.B., a 27-year-old housewife who had had rheumatic fever and scarlet fever during childhood, had dyspnea so severe that she had to be carried upstairs. There were frequent episodes of severe paroxysmal nocturnal dyspnea requiring 3 pillows for relief. She tired very easily and could not do housework. She had had several attacks of pulmonary edema and had been receiving digitalis for years.

Physical examination revealed a loud apical diastolic murmur, and an electrocardiogram showed right-axis deviation and atrial fibrillation.

At operation a distorted, heavily calcified mitral valve was found. It was fractured anteriorly and posteriorly, the orifice being enlarged from 0.8 to 3.0 sq. cm. Microscopical examination of the amputated atrial appendage showed subsiding myocarditis.

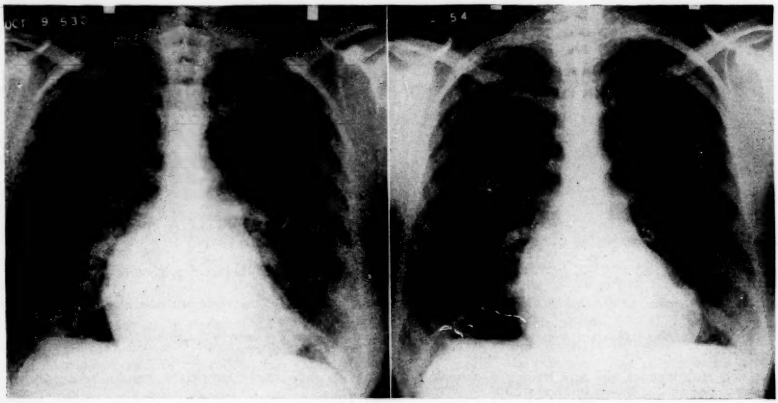
At follow-up examination 16 months after operation the patient had no symptoms and was leading an entirely normal life. She was still taking digitalis. The murmur and electrocardiogram showed no change except that she had a normal sinus rhythm.

Follow-up x-ray films demonstrated a 2-cm. decrease in cardiac transverse diameter and a smaller left atrium.

M.D., a 28-year-old housewife in the 2d trimester of pregnancy, had no history of rheumatic fever or any of its equivalents. She had marked dyspnea, as well as frequent attacks of paroxysmal nocturnal dyspnea requiring 3 pillows for relief. She coughed on exertion and had had several alarming episodes of hemoptysis; she was easily fatigued and unable to do her housework. Mild dependent edema occurred during the pregnancy, and she was taking digitalis.

Physical examination showed loud diastolic and presystolic apical murmurs.

At operation a tight mitral stenosis was found. No calcification was felt, nor was there a regurgitant jet through the mitral orifice during systole. The fused cusps were separated anteriorly and posteriorly, and the orifice was enlarged from 0.5 to 3.0 sq. cm. There was no microscopical evidence of active carditis in the amputated atrial appendage.



A B

FIGURE 3. *Films in Patient A.Z.*

Preoperative film taken on October 9, 1953 (A), *shows an enlarged main pulmonary artery, engorgement of the peripheral pulmonary vessels and an increase in the transverse diameter of the heart that was due to enlargement of the right ventricle. Measurements: transverse diameter, 15.3 cm.; long diameter 15.8 cm.; broad diameter 11.5 cm. No intracardiac calcification was seen.*

Follow-up film, taken on November 10, 1954 (B), *shows a definite decrease in the size of the pulmonary artery and the peripheral pulmonary vessels, as well as disappearance of the left-atrial-appendage shadow (this structure is amputated at operation). Measurements: transverse diameter, 14.7 cm.; long diameter, 15.1 cm.; broad diameter, 11.0 cm.*

At follow-up examination 12 months after operation the patient had no symptoms and was leading a normal life. A healthy baby had been delivered.

Follow-up x-ray examination showed a 2.5-cm. decrease in cardiac transverse diameter and a definite decrease in the size of the left atrium, pulmonary artery and right ventricle.

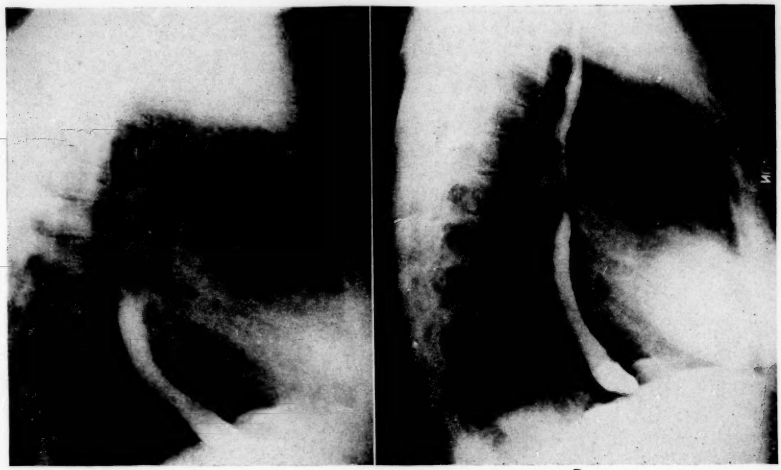
A.T., a 25-year-old man, had had rheumatic fever as a child. He had dyspnea after climbing 1 flight of stairs and had occasional attacks of paroxysmal nocturnal dyspnea, but no orthopnea; he had cough on exertion, with occasional mild episodes of hemoptysis. Palpitation was the symptom that troubled him most. He tired easily but still worked.

Physical examination disclosed a loud apical diastolic murmur, and an electrocardiogram showed right-axis deviation. The x-ray appearance is presented in Figure 2*A*.

At operation a tight mitral stenosis was found. No calcification was felt, and no regurgitation. The cusps were separated anteriorly and posteriorly, the orifice being enlarged from 0.5 to 3.5 sq. cm. No microscopical evidence

of active carditis was seen in the amputated atrial appendage.

At follow-up examination 15 months after operation the patient had no symptoms and was leading a normal life. The x-ray appearance is shown in Figure 2*B*.



A B

FIGURE 4. *Films in Patient A.Z.*
Preoperative film, taken on October 9, 1953 (A), *showing slight enlargement of the right ventricle and moderately severe enlargement of the left atrium.*
Follow-up film, taken on November 10, 1954 (B), *shows a definite decrease in the size of the left atrium.*

A.Z., a 43-year-old housewife who had had chorea during childhood, suffered from marked dyspnea — she began to wheeze after 2 stairs. There had been frequent attacks of paroxysmal nocturnal dyspnea requiring 4 pillows for relief. She had cough on exertion and had several attacks of pulmonary edema; she could do no housework. There was dependent edema up to the thigh. She was taking digitalis and mercurial diuretics and was on a low-salt diet.

The x-ray appearance is shown in Figures 3 and 4.

At operation a pure stenosis was found. No calcification or regurgitation was felt. The valve cusps were separated to enlarge the orifice from 0.5 to 3.5 sq. cm. There was no microscopical evidence of active carditis in the atrial appendage.

At follow-up examination 13 months after operation the patient had no symptoms, was leading a normal life and took neither digitalis nor diuretics.

DISCUSSION

A summary of the radiologic changes and their correlation with clinical changes is shown in Table 3. All the films were reviewed several times, and the patients were divided into groups according to whether the heart and great vessels became smaller or larger. The best results were graded + + +, and those whose hearts showed the most enlargement during the follow-up period were graded − − −. It is obvious that this grading is partly subjective and that personal opinion plays a part in it, but repeated reviews gave fairly consistent results. As is evident, the majority had little or no change, a few patients showing marked improvement or worsening.

TABLE 3. *X-Ray vs. Clinical Changes on Follow-up Study.*

X-RAY CHANGE*	PATIENTS WITH CLINICAL CHANGE†			
	+ + +	+ +	+	0
+ + +	4			
+ +	6	2		
+	6	3	2	
0	8	4	3	
−	3	2	2	
− −	2	1	1	1
− − −	1	2	1	1
Totals	30	14	9	2

*+ = decrease in size of heart or great vessels; − = increase in size.
†+ + + = maximal improvement; + + = moderate improvement; + = slight improvement; 0 = no change.

A similar review was done by the cardiologists on the basis of symptoms, murmurs and the electrocardiograms; they divided the cases into + + +, + +, or + improved, or unchanged. No patient was worse clinically at the time of follow-up study, and

only 2 were unimproved; 44 of the 55 patients now lead normal or almost normal lives.

Every patient who showed +++ or ++ improvement on x-ray examination (Table 3) was definitely improved clinically. The reverse was not true. Some patients who were greatly improved clinically (+++) are found in each of the x-ray groups, but there were fewer good clinical results among the patients whose hearts enlarged during the follow-up period.

Summary

Fifty-five patients who had undergone mitral valvuloplasty were studied at an interval of twelve to thirty months after operation.

Changes in the radiologic appearance of the heart and great vessels are reported. In a minority of the cases the heart and great vessels became smaller, and all these showed marked clinical improvement.

Although 44 of the 55 patients have been restored to normal, or almost normal, life, the majority showed no decrease in heart size, and, in a few, the heart was definitely larger.

I am indebted to Mr. Frank Johnson, of Lincoln, Massachusetts, for his advice and help in the construction of the turntables.

SOME SURGICAL ASPECTS OF MITRAL STENOSIS

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BOSTON

As a surgeon, it is my purpose to review the operative and late results in patients who have had valvuloplasty for mitral stenosis. In addition, I should like to review a few technical maneuvers that improve the *quality of valvuloplasty.*

Operative Mortality

The improving operative mortality is correlated with better prevention of emboli. This reduction of emboli is largely due to technical improvement in the management of the clotted atrium and calcific valve rather than to temporary head-vessel occlusion. Improved preoperative and postoperative care has contributed to safer surgery and better late results, but this is a thesis in itself.[1]

The operative mortality must be reported in terms of the generally accepted classification:

Group 1 patients (the benign group) are those with the murmur of mitral stenosis but no disability or symptoms.

Group 2 patients (the stable group) have the murmur of mitral stenosis and slight, nonprogressive disability.

Group 3 patients (the hazardous group) are those in whom the clinical and roentgenographic evidence of mitral stenosis is definite and whose symptoms are progressive. These patients are losing their ability to compensate for the mitral block. The progressive symptoms may be dyspnea, pulmonary edema, hemoptysis or peripheral edema, or all four. These patients can be brought into the compensated state for operation.

Group 4 patients (the terminal group) are those with classic mitral stenosis and persistent decompensation that may be stable or progressive in spite of medical treatment.

For purposes of brevity I shall combine the patients who have been operated upon in Group 2 (since there have been less than two dozen) with Group 3 and separate them from the terminal, or Group 4, patients. I have never operated on a patient in Group 1 and have had but limited experience in Group 2. With a total experience of over 1000 operations, it is possible to present statistically significant results. In the first 100 patients the mortality in Group 3 was approximately 14 per cent, whereas in Group 4 it was well over 30 per cent. Almost immediately after the first 100 operations the mortality in Group 3 dropped and ranged between 2.7 and 6 per cent in the second, third, fourth and fifth 100. The mortality in Group 4 ranged between 20 and 25 per cent in the same period. In the sixth, seventh, eighth and ninth 100 patients the mortality in Group 4 has not gone below 16 per cent. *In Group 3 it has decreased,* however, *to less than 0.5 per cent.* Perhaps one should not be so distressed with a mortality of 16 per cent in terminal patients. These are dying people. If any cancer surgeon could salvage over 80 per cent of his patients, he would be delighted. Cardiac surgeons cannot derive this satisfaction because all Group 4 patients were once Group 3 patients. By the misfortune of progression from Group 3 to Group 4 the mortality rate has multiplied fortyfold. *Herein is defined a grave responsibility for all who see patients with mitral stenosis.*[2] All who have any connection with the recommendation of surgery should realize that if a patient goes from Group 3 to Group 4 his mortality mounts disastrously. Even this is really viewing the problem in but one dimension. Dr. Ellis and his associates[3,4] have conducted the most exhaustive long-term follow-up study

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of these patients and have recently reported on the first 500 patients. Not only is the Group 4 mortality shockingly higher than that of Group 3 but also far better rehabilitation is encountered in Group 3. Many of the Group 4 patients have irreversible changes in the liver, lungs and myocardium. In the first 500 patients more than 75 per cent of Group 3 were improved, whereas only about 55 per cent were improved in the Group 4. These figures are slightly slanted in an unfavorable direction by inclusion of high mortality figures of the initial experience. The second 500 will apparently show, in a similar follow-up period, that over 90 per cent of the Group 3 patients and more than 65 per cent of the Group 4 are improved.

In short, though the operative mortality has been reduced, in selected patients, to less than 0.5 per cent and their long-term improvement elevated to more than 90 per cent, human inertia can still permit the most favorable candidates to deteriorate to the terminal stage, where the operative risk is forty times higher and the rehabilitation poorer.

Pathologic Anatomy of Mitral Stenosis

In addition to the pathologic patterns recognized as far back as the late 1940's it is now realized that secondary stenosis may exist. *Primary stenosis* is caused by leaflet fusion, and *secondary stenosis* is due to fusion of the chordae tendineae or papillary muscles or both. At times even if primary stenosis (leaflet fusion) is corrected, secondary stenosis remains beyond the leaflets. In other words, mitral stenosis can be caused by fusion of the leaflets, the chordae, the papillary muscles or all three. This is why one must think in terms of valvuloplasty rather than simple opening of the commissures, or "commissurotomy."

Either *primary* or *secondary* stenosis may be complicated by calcification. It is the calcific embolus arising from the calcified valve that is the surgeon's *bête noire*. Cerebral-vessel occlusion for a minute after the fracture is in order if it is necessary to fracture through calcified tissue. Generally, the experienced surgeon can carry his fracture or incision (with the No. 9 valvulotome) where there is no calcium. If it is necessary, however, to break through calcific "stalactites and stalagmites," one should appropriately occlude the head vessels. If the posterior-fusion bridge resists fracture, the surgeon may change positions with his first assistant, move around to the opposite side of the table and fracture or incise the posterior-fusion bridge from the patient's ventral surface. This corresponds to using an anterior operative approach.

Small, Absent or Thrombosed Atrial Appendage

Much has been said about operating through the pulmonary vein. Unhappily, this approach, which was mentioned in an article on mitral valvuloplasty by Harken et al.[5] in 1948, is difficult indeed and attended by the hazard of fracturing into the atrium or sacrificing the vein. The vein is no longer used even when the appendage has been removed at previous operation or when there is extensive clot. A zone is circumscribed on the atrial surface with two or more opposing purse-string sutures. A small stab wound is made in the circumscribed zone, the sutures being carefully avoided. The atrial wall and the clot are pierced; a Kelly clamp is then thrust into the atrium and loose clot flushed or sucked out. An open-end glass suction tip is pushed through the channel that will be taken by the finger. The cardiotomy site is next dilated with the small finger; finally the small finger is removed, and the right index finger inserted. Hemostasis is effected by traction on the opposing purse-string sutures. No "inoperable appendages" or "inoperable atria" have been encountered since the first 50 cardiotomies. The operation has been completed on all patients, some of whom have been abandoned in other institutions because of the fear of transversing the clot. These "difficult" patients have not had emboli. This technic is probably safe.

Calcification of Mural Thrombus

Calcification of a mural thrombus is generally eggshell in type and lies just inside the atrial endocardium. This condition is handled as in noncalcific atria; care is exercised not to fracture the atrium itself as one passes through the calcific zone. Sometimes, dissection is carried along the calcific atrial clot and then into the atrial chamber in a zone free of calcium.

What does one do with a calcified valve that is so "completely calcified that no fracture or no mobilization can be effected"? It was thought that 3 such valves were present in the first 100 operations. In the last 800 this situation has not been encountered. Careful palpation has always discovered a crack or crevice between leaflets, papillary muscles and chordae tendineae that could be fractured so that leaflet mobilization could be brought about. The surgeon will find that, with more thought, care and experience, there are fewer of these "impossible situations." Pathologists often present patients' hearts at staff meetings or clinical conferences with these "inoperable lesions." "Nothing could have been done about it" is the comforting cliché. It has been possible to fracture these valves consistently and to bring about leaflet mobilization. This is in direct contradiction to general clinical and pathological concepts. The "inoperable situation" is a relative term and a function of the surgeon's experience.

Discussion

With apology for telling roentgenologists about the roentgenograms and internists about cardiology, I, as a surgeon, who has "learned by being burned," should like to review a few diagnostic crutches.

First, reference is made to the roentgenograms of mitral stenosis. It is very important to see a giant pulmonary artery and congested lung fields. In the lateral view there is the large right ventricle hugging the sternum. The atrium is characteristic in mitral stenosis and quite unlike that of mitral insufficiency. The atrium of mitral stenosis is high and only moderately enlarged, whereas that of mitral insufficiency is large and sometimes aneurysmal and extends down to the diaphragm in a long, continuous sweep. This characteristic contour in mitral insufficiency is probably because the regurgitant jet thrusts posteriorly, whether initially due to relative or absolute loss of substance, and impinges most vigorously on the atrium posteroinferiorly. This force in the atrium just above the upper ridge of the ventricle may cause dilatation of the atrium. As the atrium distends it tends to gravitate downward and comes to rest on the diaphragm. This migration causes direct herniation of the annulus; this, again, further shortens the leaflets and increases the insufficiency. This increment of regurgitation causes more dilatation of this particular region of the atrium; the further dilatation and herniation cause more insufficiency. Thus, a self-aggravating, localized pathologic process explains the characteristic roentgenologic and pathologic pattern of mitral incompetence.

Now, with apologies, a few comments on auscultation. When there is a loud, booming mitral first sound, it is characteristic of mitral stenosis, compensated mitral insufficiency, aortic-valve disease or hypertensive cardiovascular disease. A "mushy" first sound is not likely to be heard in mitral stenosis. There can be a loud mitral systolic murmur with no insufficiency at all. A high-pitched mitral systolic murmur may be associated with low volume of regurgitation whereas a low-pitched murmur may accompany a large volume of regurgitation. A child's balloon deflating very rapidly may not make a loud sound, whereas one with a small leak may produce a very loud, high-pitched squeal. Indeed, occasionally, a loud mitral systolic murmur is heard, and no regurgitation is found at operation. This systolic murmur may be due to intraventricular eddy currents in systole. Just as the systolic murmur may be insignificant, many cases of extreme mitral insufficiency with no stenosis have been attended by loud, long, rumbling Grade 4 diastolic murmurs. This is probably because a completely insufficient mitral annulus lying between a giant atrium and a large ventricle may produce the same eddy currents that characterize stenosis in the presence of smaller adjacent chambers. A loud pulmonic second sound characterizes the pulmonary hypertension of mitral stenosis whereas it is not often heard in insufficiency.

A final diagnostic feature worth mentioning is the palpatory evidence of enlargement of the right versus the left ventricle. This was brought to my attention by Mr. Andrew Logan, F.R.C.S., a distinguished thoracic surgeon from Edinburgh. He points out that a thrust felt under the xiphoid may indicate enlargement of the right ventricle. If the thrust is palpated in the anterior axillary line, it indicates enlargement of the left ventricle. This Logan sign, for which he disclaims credit, is a good one. One should also learn to palpate the pulmonic outflow tract and pulmonary-valve closure through the impulse as transmitted to the chest wall.

Conclusions

It is hoped that these superficial comments on the pathologic anatomy of mitral stenosis may help explain some characteristic clinical and roentgenographic features. It is further hoped that it can be agreed that "operations for mitral stenosis" vary both in *safety and quality*. And finally, all — roentgenologists and surgeons alike — must recognize their grave responsibility for bringing patients to surgery when the risk is less than 1 per cent in operation and the rate of rehabilitation is excellent.

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A SECOND OUTBREAK OF BOSTON EXANTHEM DISEASE IN PITTSBURGH DURING 1954*

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A PREVIOUS report[1] described an unusual epidemic exanthem that occurred during the late summer of 1951 in Boston. Evidence then available indicated that the illness represented a clinical entity different from the more commonly known exanthems. In addition, the isolation of a new group of transferable agents from feces of several of the patients, as well as their neutralizing-antibody responses, suggested a possible etiologic relation of these agents to the disease.

These initial observations have now been corroborated and extended by studies of a second outbreak of a similar clinical entity observed in Pittsburgh during June to September, 1954. Filterable agents that appeared to be similar to those isolated from patients of the first outbreak in Boston were found in association with the disease in Pittsburgh. This report presents epidemiologic and clinical features of the exanthem disease as observed in 1954 during a small outbreak in a residential suburb as well as among scattered cases occurring in different areas of the city. Summarized results pertaining to isolation of agents and serologic tests in tissue cultures are included here, but details of this information will be presented elsewhere.[2]

METHOD OF STUDY

Attention was first called to the current exanthem outbreak in June, 1954, by the occurrence of an illness similar to German measles in a six-year-old child, who had had typical rubella several months previously. The illness was suspected of being the recently reported epidemic exanthem[1] by Dr. Bertram Girdany and called to my attention through the courtesy of Dr. Horace Gezon. Several subsequent patients were kindly referred by Dr. William Stengel, as well as by Dr. Bernard Michels and Dr. Sidney Saul, all of Pittsburgh.

When the initial case was investigated, it was found that additional members of the same household were also affected; further inquiry disclosed that similar illnesses were present in neighboring families. The outbreak was followed by detection of cases, examination of patients and collection of appropriate specimens during repeated home visits. Later, scattered patients in different areas of the city were referred by pediatricians and studied in the same manner. Only 1 patient, who had a convulsion at onset, was hospitalized.

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Aided by a grant from the National Foundation for Infantile Paralysis.

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Specimens of feces, throat washings and blood clots were tested for presence of cytopathic agents in roller-tube cultures of monkey-kidney and testicular tissue. Serum samples in serial twofold dilutions were tested in similar cultures for presence or absence of neutralizing antibodies. Methods for these procedures were similar to those previously reported.[3]

EPIDEMIOLOGIC OBSERVATIONS AND CASE REPORTS

Suburban-Community Outbreak

The residential area in which the first case was detected was composed of approximately 31 homes located about 8 miles south of the center of Pittsburgh. This suburban community comprised a distinct group-

TABLE 1. *Epidemic Exanthem Disease in a Suburban Community in Pittsburgh, Pennsylvania, 1954.*

TYPE OF PATIENT	APPROXIMATE POPULATION	DEFINITE CASES*	PROBABLE CASES†	RATE OF OCCURRENCE
Adults (>18 yr.)	60	6	0	6:60 (10%)
Children (<18 yr.)	46	7	4	11:46 (24%)
Totals	106	13	4	17:106 (16%)

*Based on clinical diagnosis plus isolation of cytopathogenic agent or rise in neutralizing-antibody titer to immunologically related agent, or both.

†Based on clinical findings; no laboratory data available.

ing of dwellings that was partially, though not completely, isolated from adjacent residential areas. There was no crowding of houses, but generally free and unrestricted association between children of the different households existed.

The population within this residential area under consideration consisted of 60 adults and 46 children. Most of the adults were less than fifty years of age, and the great majority of children were less than ten years old.

Within this population group, a total of 17 patients were found to have an illness that justified the diagnosis of the epidemic exanthem on the basis of typical clinical picture or clinical as well as laboratory findings. The cases occurred over a twelve-day period during the month of June. Eleven of the patients were children, ranging in age from five months to nine years, and six were adults twenty-eight to thirty-five years old. Cases occurred in 10 of 31 households. There were 4 cases of multiple illnesses within a single household, 3 involving an illness in 1 of the parents as well as children. Table 1 summarizes information on the prevalence of the disease in this residential suburb. Further data on the epidemiologic pattern

of the outbreak are presented in Figure 1. In this community, 10 per cent of the adult population and 24 per cent of the children were found to have evidence of the infection. The over-all observed rate was 16 per cent, with 32 per cent of the households involved. The actual frequency of the disease was likely even higher than indicated by these data, since

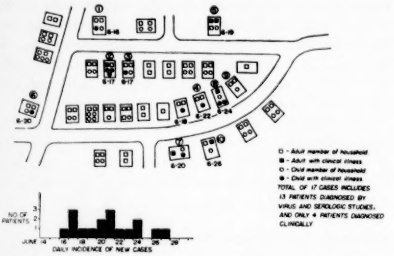

FIGURE 1. *Map of Suburban Community in Which the Epidemic Exanthem Occurred, Showing the Epidemiologic Pattern (Total Population, Date of Onset of First Case and Number of Cases in Each Household).*

3 additional cases not included above were suspected on the basis of history.

Clinical Summaries

Suburban Case 1. D. McG., a 4-year-old boy, complained of "stomach ache" and was found to have a temperature of 102°F. by rectum during the afternoons of June 17 and 18. The mother thought the child's eyes appeared bloodshot, but there were no further complaints. During the evening of June 19 a skin eruption appeared, mainly on the face and chest. A fading rash was still present 3 days later, when physical examination was otherwise negative.

Suburban Case 2. R. McG., a 6-year-old male sibling, also had a temperature of 102°F., "stomach ache" and reddened eyes on June 17 and 18. Two days later a rash appeared over the face and trunk. When examined 48 hours later, the patient no longer had a rash and other findings were normal.

Suburban Case 3. S. McG., a 5-month-old female sibling, became irritable on June 21 and was found to have a temperature of 102.8°F. by rectum. Later during the same day a generalized faint rash was interpreted by the mother as a heat rash. On the next morning the temperature was 101°F., and examination late in the same day disclosed a mild but definite rash of pink maculopapules 2 or 3 mm. in size. The eruption was distributed mainly over the face, arms and trunk. One large lymph node was palpable in the left occipital region. The rash faded in 2 days.

Suburban Case 4. J. McG., the 29-year-old father of the family, experienced fever, frank shaking chills, severe frontal headache and a slight sore throat on the evening of June 21. Weakness and prominent aching of joints and back muscles were also present. The same symptoms, as well as burning sensation of the eyes, were present the next day, and the temperature was 102°F. by mouth. A diagnosis of "flu" was made by the family physician, and chlortetracycline was started. Examination in the late afternoon of June 22 showed a temperature of 104°F. and an acutely ill man, who was flushed and sweating. The throat was moderately red, with a small, raised area, but no vesicles, on the left tonsillar pillar. There was no adenopathy or skin rash. Chills, headache and sore throat continued on the following day, and drowsiness was noted. On June 24 he felt much better; the temperature was normal, and the pharynx appeared normal. In the evening of the next day he noted a rash over the abdomen, and 1 day later a definite eruption of faint and mottled, small, macular lesions was still present over the anterior abdomen, but nowhere else on the body. The rash disappeared the next day and recovery was uneventful.

The mother of the family remained well. However, on June 19, the McG. family was visited for several hours by relatives, including 2 children less than three years old. This was the only previous recent contact between the two families since they lived about 5 miles apart. Four days later a mild febrile illness developed in both children of the visiting family, with a skin rash described as similar to that seen in the McG. children.

Occurrence of Scattered Cases in Different Areas of the City

After recognition of the epidemic exanthem in the suburban community, additional patients with suspected cases were referred by Pittsburgh pediatricians during the subsequent months of July, August and September, 1954. The new group of patients studied came from widely scattered areas of the city. In 4 different households a total of 7 cases were found that appeared, on the basis of both clinical and laboratory findings, to represent the same exanthem disease. The 4 households were located at least 3 miles apart, and in only 1 was there a history of possible indirect contact with a patient from the earlier outbreak in the suburban community.

Brief clinical summaries of 2 cases from among the scattered cases are given below. One of the patients was hospitalized*; all others were seen at home.

City Case 1. E. N., a 1-year-old boy, became irritable on June 27, and ate poorly, and the mother noted that his eyes were reddened. These symptoms continued until June 30, when fever developed (temperature not recorded), and the onset of a skin eruption was noticed. When the patient was seen on July 1 a prominent, generalized rash was present. The lesions were red, slightly raised, varying from a few millimeters up to 1 cm. in size, and in some areas confluent lesions produced a blotchy appearance. The rash lasted for 4 days. The patient had had classic roseola 4 months previously with a rash less prominent than that with the current illness and involving only the trunk and neck.

Subsequent follow-up history revealed that 4 children from 1 family, 2 months to 8 years of age, and 2 children less than 4 years old from another family had all attended a birthday party for patient E.N. on June 28. Five days later every one of the 6 contacts had an illness characterized by slight fever and a skin rash on the face, arms and neck.

City Case 2. E. W., an 8-month-old male infant, was found to have a temperature of 101°F. in the early afternoon of July 25. When the temperature rose to 104°F., penicillin was given, and a few hours later a generalized convulsion occurred. The patient was given phenobarbital and more antibiotics, and was admitted to the hospital at 11 p.m., when he had a temperature of 102°F., slight red-

*The findings in this case were kindly made available through the courtesy of Dr. Sidney Saul and the Montefiore Hospital, Pittsburgh, Pennsylvania.

dening of the right eardrum, supple neck and normal mucous membranes. Aspirin and sponge baths were given, and by the next morning the temperature had dropped to 100.4° F. A rash was noted on the morning of July 27, and the temperature rose to 102.4°F. that afternoon. In spite of aspirin and sponging on the following day, the temperature reached 103.8°F. The rash at this time was a generalized maculopapular eruption involving even the soles of the feet. The fever had subsided by July 29, but the rash persisted for 2 more days. There were no other pertinent physical findings. Examination of the spinal fluid and urine was negative, as was x-ray study of the lungs and heart. Blood white-cell counts were normal on 2 occasions.

It was learned that the patient's 5-year-old sibling had had a skin rash on July 23 and 24, but no noticeable fever. In addition, a niece manifested a similar skin eruption on July 28.

Clinical Features of the Exanthem Disease

When the cases from the suburban-community outbreak were added to the scattered cases that occurred later, a total of 24 patients with the exanthem disease were available for clinical analysis. Sixteen were children, two-and-a-half months to nine years old, and nearly a third of these were one year or less. The remaining 8 patients were adults ranging in age from twenty to thirty-six years. Most adult patients were parents whose children were also affected.

Incubation Period

In 2 cases it was possible to make reliable estimates regarding the incubation period of the exanthem disease. The interval between contact with the McG. family and onset of symptoms in visiting relatives was four days, and with the birthday-party contact of patient E.N., the corresponding interval was five days. In 6 other family outbreaks, the duration between onset of symptoms in primary and secondary cases was usually three to four days, and as long as six to seven days in 1 case.

Symptoms and Clinical Picture in Children

In infants one year of age or younger, the first evidences of the illness almost invariably were irritability and fever. Older children also usually had temperatures of 101 to 103°F. that seldom lasted for more than two days. However, maximum temperatures of 104°F. were recorded in 2 patients, and were associated with a convulsion in 1. Some complained of mild sore throat, headache and "stomach ache," or showed a poor appetite. Children commonly continued to be up and about playing even though they had fever and symptoms, but some were listless and tired. Reddened eyes at the onset of the illness were noted by mothers of several patients, but this was not a notable finding when children were examined at the time of the rash.

In most cases, the rash appeared within several hours up to a day after the fever and other signs or symptoms had subsided. Frequently, there was a day of freedom from symptoms before onset of the rash. However, several patients were still febrile when the rash appeared.

The skin eruption was easily detected in all children although it varied considerably in extent. It was generalized in many patients, with the main distribution over the face, chest and back, and to a lesser extent upon the extremities. The buttocks were also often involved. The lesions were pink, not as deep or dark of those of measles, slightly raised and about 2 to 4 mm. in size, with rather indistinct borders. Frequently, they presented a pebbled appearance of the skin. When extensive, the lesions were confluent and somewhat similar to the blotchy rash of measles. In the usual case, however, the eruption resembled that of rubella. Pruritus was never present, and the rash lasted for two to four days.

Adenopathy was never very prominent or generalized, although a few moderate-sized, firm occipital or posterior cervical lymph nodes were commonly palpable. No sequelae or recurrences were noted after disappearance of the rash.

Symptoms and Clinical Picture in Adults

In contrast to the usual mild illness in children, the epidemic exanthem disease was symptomatically more severe and clinically quite different in adults. The onset of disease was abrupt and easily established in all the cases except 1, in which symptoms were vague, mild, and gradual in development. Initial symptoms in all 8 adult patients included chills, headache and muscle aches and pains. In most cases temperatures of 101 to 104°F. were recorded, but 2 patients who did not take their temperature noted no obvious fever. Adults commonly complained of burning or pain in the eyes. Definite evidence of prostration was present in several of the patients, who reported that they felt weak, tired or drowsy. Less common symptoms were sore throat and crampy abdominal pain. In 1 case the abdominal cramps were associated with diarrhea. Symptoms lasted only about forty-eight or at most seventy-two hours.

Physical findings during the symptomatic phase of the disease were uniformly negative except for the rash in some patients, or moderate pharyngeal injection and mucous-membrane findings, which are discussed below. There was no significant adenopathy.

In 4 of the 8 adult patients a rash developed within two to five days of the onset of symptoms. In all patients with a rash, the skin eruption appeared after fever and acute symptoms had subsided. The rash was scanty, macular in character and distributed over the abdomen, legs or face and upper arms, and lasted only twenty-four to thirty-six hours.

Mucous-Membrane Lesions Observed in Some Patients

Fifteen patients, 6 of them adults, received a thorough examination of the pharynx at some time during the course of the disease. In these cases, the throat was examined after symptoms of illness were already well established or after the rash had already appeared. Many patients exhibited moderate pharyn-

geal redness, but 7 had additional findings. Tiny, yellow-white, raised, miliary-type lesions were noted on the soft palate or uvula of 2 adults and 1 child. Another type of lesion, consisting merely of single or multiple raised, reddened areas on the soft palate or tonsillar pillar, was seen in 1 adult and 2 children.

TABLE 2. *Results of Attempts to Isolate Virus and Serum Neutralization Tests from Pittsburgh Patients.*

PATIENT	AGE	VIRUS ISOLATION	NEUTRALIZING-ANTIBODY TITER*		
			DATE	DAY OF DISEASE	TITER
Community outbreak:					
L.L.	6 yr.	Not done	6-24-54 7-13-54	9 28	8 32
D. McG.	4 yr.	+ (feces)	6-22-54 7-13-54	6 27	4 16
R. McG.	6 yr.	+ (feces)	6-22-54 7-13-54	6 27	4 16
S. McG.	5 mo.	+ (feces)	(Blood not obtained)		
Mr. McG.	29 yr.	+ (blood, throat & feces)	6-22-54 7-13-54	2 23	<2 8
T.F.	5 yr.	+ (feces)	6-22-54 7-13-54	5 26	2 8
Mrs. W.	29 yr.	+ (feces)	6-22-54 7-15-54	4 27	2 8
Mr. W.	30 yr.	+ (feces & throat)	6-22-54 7-13-54	2 23	2 16
Mrs. B.	28 yr.	+ (feces)	6-26-54 7-13-54	4 21	2 32
K. Wel.	6 yr.	+ (feces)	6-26-54 7-13-54	3 20	<2 8
R. Wel.	5 yr.	+ (feces)	6-26-54 7-13-54	3 20	<2 8
Mrs. Wel.	30 yr.	Negative (throat)	6-28-54 7-13-54	2 17	<2 32
Mr. D.	35 yr.	+ (feces)	6-28-54 7-13-54	3 18	<2 32
Scattered cases:					
E.W.	8 mo.	+ (feces)	7-29-54 (No convalescent-phase blood obtained)	5	<2
E.N.	1 yr.	+ (feces)	7- 1-54 7-15-54	4 18	<2 8
A.J.	2½ mo.	+ (feces)	(Blood not obtained)		
Mrs. J.	36 yr.	+ (feces)	8-11-54 8-28-54	5 (?) 22	4 8
B.T.	2 yr.	+ (feces)	9-13-54 10- 1-54	5 (?) 23 (?)	4 16
A.R.	7 mo.	+ (feces)	9-13-54 10- 1-54	3 20	2 4
Other case†:					
J.P.	2½ yr.	+ (feces)	(Blood not obtained)		

*Tests in tissue culture vs. agent isolated from Pittsburgh patient R. Wel.; titer represents reciprocal of serum dilution.

†Patient contact of McG. family; illness with rash developed 4 days after exposure.

Finally, both types of lesions were present in the throat of 1 child. No vesicles or ulcers were noted. Therefore, an enanthem may also be present in patients with the epidemic exanthem disease.

LABORATORY FINDINGS

Specimens from a total of 19 patients with epidemic exanthem were tested in tissue cultures, and cytopathic agents were recovered in 18 cases. Eleven of the patients with positive isolations were from the group in the suburban-community outbreak, 6 were from the scattered cases in different areas of the city, and 1 was a contact of family McG. of the community outbreak. The agents were recovered, in most cases, from fecal specimens collected within two to ten days of the onset of illness. Samples from throat garglings of 2 patients were positive. In 1 patient (Mr. McG., whose clinical summary is presented above) recovery of an agent was made from the blood drawn on the second day of illness when the patient had a temperature of 104°F.

All isolates from Pittsburgh patients produced the same type of cytopathogenic effects in roller-tube cultures; moreover, the changes in tissue culture were similar in appearance to those induced by agents isolated in 1951 from the patients in Boston.[3,4]

Tests for neutralizing antibodies against 1 of the Pittsburgh isolates were performed on samples of acute-phase and convalescent-phase serums from 16 patients. In 14 of the 16 cases, it was possible to demonstrate a fourfold or greater rise in neutralizing-antibody titer in convalescent-phase as compared to acute-phase blood specimens.

Results of laboratory tests are summarized in Table 2.

COMPARISON OF EXANTHEM DISEASE IN PITTSBURGH AND BOSTON

The Pittsburgh exanthem disease showed striking similarities to the unusual epidemic exanthem that occurred in Boston in 1951.[1] A more detailed comparison of features that characterized the two outbreaks in different cities was therefore made (Table 3).

Findings for the two outbreaks were practically identical so far as estimated incubation period, symptoms of disease, initial diagnoses of cases by physicians, as well as names given the illness in children by parents, type of rash and clinical evidence of communicability were concerned. Fewer adult cases were available for study in Boston than in the Pittsburgh outbreak, but, in the former city, unrecognized cases in adults without rash were suspected. The only discrepancy was in the different types of mucous-membrane lesions observed in a minority of patients from both outbreaks.

Of particular interest is the fact that agents transferable in vitro were recovered from a high proportion of patients in both cities. Furthermore, nearly all patients studied serologically from both areas manifested rises in neutralizing antibodies to one or more agents recovered in association with the illness in the respective locality.

DISCUSSION

From the data presented, there appears little doubt

that the 1954 Pittsburgh exanthem constituted a specific entity unlike other commonly known eruptive diseases. In addition, the clinical, epidemiologic and laboratory evidence indicates that the exanthem disease in Pittsburgh represented the same illness recently reported from Boston.[1]

The incidental finding of mucous-membrane lesions in some cases of the epidemic exanthem disease is of doubtful significance. Several of the patients in the Boston outbreak[1] were reported to have pharyngeal or palatine vesicles that progressed to tiny punched-out ulcers of the type described for herpangina,[5] whereas two different varieties of less distinctive pharyngeal findings were noted in 7 patients in Pittsburgh. It should be recalled, however, that a concurrent Group A Coxsackie virus infection was implicated in at least 2 of the Boston patients who had mucous-membrane lesions. Yet it is possible for some type of mucous-membrane lesion to be associated with the exanthem disease. The absence of consistent mucosal lesions may have been due to the fact that patients were generally not examined in the early stages of the disease. Observations thus far, however, indicate that mucous-membrane lesions are not always present, and if there is an associated enanthem, it is not distinctive in character.

Several of the more outstanding features of the newly recognized epidemic exanthem disease deserve emphasis. First, the incubation period of three to seven days is short in comparison to that for rubella and measles. This is useful in clinical differentiation, but when individual or scattered cases of the new exanthem disease occur, they are very difficult to distinguish from rubella, roseola infantum and perhaps occasionally even from measles, without laboratory studies. Secondly, in view of the frequent occurrence of multiple cases in the household and in other contacts, clinical infection with the epidemic exanthem appears to be readily communicable. Finally, the occurrence of the exanthem disease in adults as well as in children, and the somewhat different clinical picture in the former, should be kept in mind for aid in recognition of the disease. This distinction is particularly important when there has been no known contact with childhood cases.

TABLE 3. *Comparative Features of Outbreaks in Boston and Pittsburgh.*

OUTBREAK	AVERAGE INCUBATION PERIOD	DIFFERENTIAL DIAGNOSIS	DEFINITE CASES IN CHILDREN				DEFINITE CASES IN ADULTS				MUCOUS-MEMBRANE LESIONS	COMMUNICABILITY	ETIOLOGIC STUDIES	
			NUMBER	AGE GROUP	MAIN SYMPTOMS	RASH	NUMBER	AGE GROUP	MAIN SYMPTOMS	RASH			ISOLATION OF AGENTS	ANTIBODY RESPONSE TO TISSUE-CULTURE AGENTS
	days			*yr.*				*yr.*						
Boston (1951)	3-8	Rubella, roseola infantum & "heat rash"	13	4/12-8	Irritability & fever	Present in all	2	26	Chills, fever, muscle aches & pains, headache & sore throat	Minimal*	Vesicles & small ulcers in about 20%	High; multiple cases in households.	Positive for 7 of 8 patients tested in tissue culture	Positive in 10 of 11 patients tested
Pittsburgh (1954)	3-7	Rubella, roseola infantum & "heat rash"	16	2/12-9	Irritability, fever, sore throat, headache & "stomach ache"	Present in all	8	20-36	Chills, fever, muscle aches & pains, headache, sore throat & abdominal cramps	Minimal†	Varied & nondescript in about 30%	High; multiple cases in households.	Positive for 18 of 19 patients tested in tissue culture	Positive in 14 of 16 patients tested

*1 of 2 cases.
†4 of 8 cases.

Numerous inquiries and comments have indicated the desirability of assigning a name to the exanthem disease described. The nosology of contagious diseases characterized by a skin eruption is already confusing, particularly those designated by number in the older literature, as well as the diseases whose names are closely related. A nomenclature based on specific etiology would be ideal, but unfortunately most of the exanthemas are firmly fixed in both lay and medical terminology by decades of accepted use. In view of the fact that the first outbreak of the newly recognized disease occurred in and around Boston and was also first studied there, it is proposed that the disease be referred to as "Boston exanthem."

SUMMARY

An infectious exanthem that occurred as an epidemic in a small suburban community as well as in scattered sporadic cases during 1954 in Pittsburgh is described. The illness affected adults as well as children and was characterized chiefly by several days of fever and a rash lasting one to three days. Clinical

and epidemiologic features of the disease compared very closely to the unusual epidemic exanthem reported previously in Boston. Agents cytopathogenic for tissue cultures were isolated, and a related neutralizing-antibody response was associated with the disease in the patients studied. Available evidence indicates that the exanthem disease in Pittsburgh represented the second outbreak of a newly recognized clinical entity. The name "Boston exanthem" is proposed for this disease.

I am indebted to Dr. Jonas E. Salk, who provided facilities and support during the course of the studies described.

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SPECIAL ARTICLE

"AND THE WATERS PREVAILED"

Public-Health Aspects of the 1955 New England Flood

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PHILADELPHIA

ON August 17, 1955, hurricane "Diane" was declared dead by the Weather Bureau. During the following two days, more than 12 inches of rain fell on much of New England, New York and Pennsylvania. This is usually the equivalent of more than 10 feet of snow!

Civil Defense organizations, which have taken over most of the handling of civilian disasters, were alert and on the job on the morning of August 19, when weather reports indicated that the rain would stop by noon. However, the rain continued with increased intensity until about 4 p.m. Much of the damage done occurred in this period or even after the rain had stopped, when saturated ground, filled sewers, full river banks and water reservoirs could hold no more and water overflowed river banks, bursting dams, washing out roads, flooding streets, cellars and lower floors of buildings, washing away buildings and utilities and covering all low-lying areas (Fig. 1).

In the 1953 tornado, damage was all above ground, with utilities unaffected and few health problems created. In the 1955 flood, damage was on or below ground. Many problems resulted.

Water Supply

Although many private and public water supplies in the small towns were incapacitated, in the City of Worcester no breaks occurred in the lines. There was a slight drop of pressure in the higher areas when hydrants were opened to relieve the pressure on the Lynde Brook dam. This drop in pressure was not great enough to cause concern over back siphonage in submerged inlets or inward seepage through leaks. Multiple tests showed the water to be safe.

Potable water was sent to some of the towns in clean 40-quart milk cans and in milk tank trucks. Recommendations that local water be boiled before use were made public.

Typhoid Hazard and Immunizations

Rumors spread rapidly that typhoid inoculations were necessary for the entire population. It has been impossible to trace the origin of this belief, which went so far as to hold that check points had been set up on some roads beyond which no one who had not had an injection would be permitted to pass. No such recommendation had been made by any responsible public-health official.

FIGURE 1. *Appearance of the City during the Flood.*

Typhoid immunization requires three injections a

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week apart and an additional period for immunity to build up. The incubation period is almost always shorter than this. Typhoid inoculations have no value in a flood for persons who do not continue to be exposed to contaminated water supplies.

The probability of typhoid contamination by flood waters in this area was so small mathematically as to be immeasurable. Only 5 carriers and no cases were known in the area. The volume of water was not measurable, but the dilution factor was fantastically tremendous in the general flood waters and extremely great even in basements where sanitary sewers backed up.

FIGURE 2. *Disposal of Contaminated Food.*

ELECTRIC POWER

Power failures were widespread except for the city. Private power generators were hard hit since many were in basements that were flooded. Early warnings to raise or remove motors to higher levels were generally heeded, but because the depth of the flood had not been anticipated, even the higher levels were submerged. Motors required baking before they could again be used.

Dry ice was brought in to protect frozen foods. However, the impassibility of roads prevented its being brought to many needed areas.

ROADS, COMMUNICATIONS, PUBLIC FEEDING

Relatively little need was encountered for public feeding despite the cutting off of supplies because of washed out and submerged roads. Roads and other communications were rapidly re-established.

FOOD

By far the greatest public-health problem was that of submerged food. Worcester is the wholesale distribution and shipping center for a large area. All food but that in glass or metal containers was dissolved or matted together in a conglomerate mess.

For dealing with the rest, it was decided to follow the manual that had just been issued (in June, 1955) by the Food and Drug Administration of the United States Department of Health, Education and Welfare, *Civil Defense Information for Food and Drug Officials.*

The immediate task was to secure, tag and place under quarantine all suspected food.

Canned goods and hermetically sealed glass containers were considered salvageable. All other foods were condemned for destruction.

Disposal posed a problem. The contents were too wet and the volume too great for the city incinerator. The food contents would have created a nuisance at the regular city dump. To handle this material a special site was selected at the sludge-dump area of the sewage-treatment plant, where the material was dumped, bulldozed and covered over daily (Fig. 2).

It was necessary to place potentially contaminated food under guard or to separate it from salable food. A skating arena was requisitioned for use as a warehouse. All salvageable food was brought there. Each dealer's stock was kept separate. The entire establishment was under the supervision and guard of a health-department representative.

Dealers were permitted to undertake their own salvage operations under supervision. This called for washing, chlorine immersion, rinsing, drying and relabeling. When a bonded and state-inspected salvage company appeared, none of the dealers attempted their own salvaging but sold the food to the salvage company, which rapidly moved the food out of the city to its plant.

Only one major milk plant was flooded. Collaboration among the dealers kept the milk supply at an even level.

Alcoholic beverages presented a unique problem. Temporary legislation, both federal and state, passed after the 1954 hurricanes, permitted tax rebates on destroyed stocks. Such taxes often amount to more than half the value of such stock. In the hope that similar legislation would be passed, a meeting, attended by representatives of the federal and state alcohol tax units and by the wholesale liquor dealers, was held. It was agreed to take all contaminated alcoholic beverages (Fig. 3) to the sludge dump for destruction by the bulldozer. A tax representative and an agent of the health department were to verify and certify inventories destroyed.

The amount and value of foods and beverages destroyed and salvaged are shown in Table 1.

HOUSING AND NUISANCES

Within the city relatively few inhabitants were rendered homeless. In the rural area it was necessary to bring in trailers as temporary shelters.

In some cases, immersion caused all furnishings, walls and so forth to become such a sodden, malodorous mess that nothing could reasonably be salvaged.

Drowned and decaying chickens and small animals, along with filth, created odors so severe that cleaning crews wore masks.

Flies, of the green-bottle or blow variety, appeared in great numbers. These were controlled by spreading of fly flakes (Malathion) in large areas.

Clothing, Paper Supplies and Mattresses

No restrictions were placed on the sale or use of submerged clothing. It was not believed that these articles presented any potential hazard.

Figure 3. *Disposal of Contaminated Beverages.*

Mattresses and paper supplies were useless after submersion and did not warrant salvage.

Discussion

It is important that the objectives of a health department in handling disasters be defined. Obviously, the department must protect the public health and safety. But this must be considered in relation to the general welfare of the community. If, in a hypothetical situation, the *only* food available had a *slight* chance of being contaminated, it could well be that the community would be better served if the consumption of such food were allowed. Standards must always be considered in relation to the circumstances. What might not be acceptable in normal times could possibly be necessary in disaster.

In a flood such as the one faced in 1955 the department's objectives were first to eliminate any possible source of disease and then to help restore normal community operations as rapidly as possible and to salvage for the community as much as possible.

Table 1. *Food and Alcoholic Beverages Destroyed and Salvaged.*

Disposal	Food		Alcoholic Beverages	
	Amount	Approximate value	Amount	Approximate value
Destroyed	921,837 lb.	$307,200	15,303 cases	$153,900
Salvaged	350,000 lb.	$117,000	None	None

Placing potentially contaminated food under condemnation and quarantine attempted to reach the first objective. Removing this food from the stores speeded the return to normal operations. Supervising and certifying to the destruction of liquor and foodstuffs helped reduce losses and increased salvage.

In many cases food stores were allowed to reopen while their basements were still being cleaned although shut off from the store and while odors from the basement were present. Normally, in a food store, any comparable malodor would cause concern regarding its sanitation.

It was necessary for the public to be aware of the cause of the odor and to know that the health department was also aware of it and sanctioned the opening of the store.

Constant reports to the public through newspapers and radio were essential to keep people informed of developments, so that they would understand instructions and co-operate in the program. Instruction for home salvage and for preservation of frozen and other foods despite power loss had to reach all concerned in the community and to reach them clearly, without distortion.

An indication of authority of source was necessary in all releases to counter the ill conceived rumors that rapidly arose. Perhaps as much emphasis was needed on what was not indicated and what should not be done as on the specific positive instructions released. Reassurance was offered on the absence of hazards from inanimate objects that might have been covered by filth and might have acquired a persistent odor. Ordinary mechanical washing was usually adequate to remove this although chlorine-releasing and organic-deodorizing chemicals were helpful.

It is interesting that the loss to flooded dealers in alcoholic beverages was decreased by the total destruction of submerged goods rather than by salvage — even if salvage had been possible. Salvage companies offered approximately 25 per cent of the cost whereas destruction saved as much as two thirds of the whole-

sale costs. In many cases, domestic manufacturers of drugs, food and liquors allowed full credit of the f.o.b. wholesale cost at the plant on receipt of adequate certification that the products had been condemned and destroyed.

It is believed that the amount of potential contamination of sealed food and liquor containers was very slight and would constitute a minimal hazard to persons ingesting the contents. Indeed, I should not have hesitated to consume such material myself. However, to set up a public policy on such a basis and officially to reassure purchasers of the safety of such products would be indeed hazardous, particularly when the manual referred to above called for destruction of this material. It was inevitable that the policy adopted should permit private individuals to use submerged material or not, as they saw fit, with the precautions recommended by the health department, but that the sale or public use of such material should be forbidden.

What recommendations can be made for the future handling of similar disasters?

Most important would be the presence, universally, of well organized health departments staffed by professionally well trained personnel.

There is an urgent need for a reservoir of *emergency funds* to permit immediate expansion of operations without resort to a great deal of legal red tape. Too often, in governmental operations, funds are too specifically earmarked in their functional use. Thus, a health department might find itself seriously delayed in expanding personnel, or in performing emergency functions not routinely budgeted for the department. Such functions could be the cleaning of sodden filth out of homes and the disposal of animals. The availability of emergency funds would make for the greatest flexibility of function in health-department operations.

In preparation for the unforeseen, flexibility should be a key objective. The unforeseen cannot be adequately predicted.

MEDICAL PROGRESS

CARCINOMA OF THE BREAST*

The Study and Treatment of the Patient

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BOSTON

THE management of mammary cancer has been at the forefront of surgical thought during the past half century. Now, the therapeutic horizon is expanding rapidly. We can offer the unfortunate woman suffering from this common disease a remarkable range of helpful measures even though she is far advanced in her illness and cure beyond our reach.

The purpose of this paper is to review the present status of work in this field, the endocrine aspects of which were last reviewed in the *Journal* by the late Dr. Nathanson in 1952.[1] Since the publication of his review, the chief areas of development have been as follows:

The "McWhirter controversy" over local treatment: radical surgery vs. simple mastectomy combined with intensive radiation.

The use of urine calcium excretion and endocrine assay as study devices to define the endocrine responsiveness of the tumor and select the proper treatment.

The recognition of ovarian cortical stromal hyperplasia in postmenopausal women as a frequent endocrine setting for the disease.

The use of cortisone in study and treatment.

The use of adrenalectomy and hypophysectomy in operative management.

The matters listed above will therefore be given special consideration here. No effort has been made to mention all the articles bearing on this subject and published since 1952. Instead, it is our purpose to present an integrated and practical approach to the disease as based on current knowledge.

This review is arranged by subjects as follows:

I. The Setting for the Disease.
II. The Nature of the Disease.
III. The Study of the Patient.
IV. The Role of Breast Surgery.
V. Endocrine Treatment: Medication and operation.
VI. Irradiation.
VII. Planning Treatment for the Individual Patient.

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I–The Setting for the Disease

The Estrogen Environment

That the disease in animals thrives best in an estrogen-rich environment is now so well known that it needs little further emphasis here. The work of Lathrop and Loeb,[2] Lacassagne,[3] Murray[4] and Geschickter[5] and many others establishes the fact. The much greater frequency in human females than in males obviously bears out the association of estrogenicity and pathogenesis.

The cyclic stimulation of the female menstrual periods has an effect on the disease, as shown in the studies of Rawson.[6] Since the majority of these tumors, in the young or menopausal woman, are sensitive to changes in their endocrine environment, such periodic "surges" of estrogen stimulation may well affect the onset of the disease as well as its course. The events at the menopause deserve closer scrutiny in this light. There is a definite relation between the development of breast cancer and the time of onset of the menopause: five times as many women with breast cancer have a late menopause as normal women.[7] Of 342 women presenting with this disease and aged fifty years or more, 54.7 per cent were found still to be menstruating.[8]

The production of estrogens in the postmenopausal period may reach a surprisingly high level, and the curve of breast stimulation then becomes constant, losing its periodicity, particularly when the ovaries show "cortical stromal hyperplasia."

Cortical Stromal Hyperplasia

Smith[9] observed an association of endometrial carcinoma with granulosa-cell tumors of the ovary and diffuse thecal-cell hyperplasia; he also noticed that 2 of these patients had an associated mammary carcinoma. He appreciated the fact that the cells frequently seen in the ovaries removed from postmenopausal women suffering from carcinoma of the endometrium were similar to the cells seen in a granulosa-cell tumor, which produce large amounts of estrogens. These changes he described as cortical stromal hyperplasia, and in the description of this association made a contribution to the understanding of this disease that is of far-reaching importance.

Sommers and Teloh[7] studied the ovaries obtained from 100 postmenopausal women with metastatic mammary cancer and noted the presence of cortical stromal hyperplasia in 86 cases. A control group of postmenopausal women without mammary cancer showed this change in only 37.6 per cent of cases. In a smaller group of postmenopausal women whose ovaries were removed before or at the time of the primary treatment of mammary carcinoma, Smith[10] found stromal hyperplasia in 91 per cent; similar results have been found by others.[11]

Smith[12] postulates that cortical stromal hyperplasia represents an attempt of the "old ovary" to respond to gonadotrophic stimulation. Since these ovaries contain no follicles, the stroma is all that remains to be stimulated. The increase, he suggests, is due not only to increased follicle-stimulating hormone (FSH) but also to a raised luteinizing-hormone (LH) level produced by "unknown factors or the cancers themselves." He points out that support of this is seen in the evidence for increased LH production caused by tissue-damaging agents.[13] The products of metabolism of the cancer itself or of protein catabolism might act in such a way as to lead to pituitary stimulation, increased LH production and the development of cortical stromal hyperplasia.

The hypothesis that ovaries showing cortical stromal hyperplasia secrete large quantities of estrogens that may stimulate, or be an etiologic factor in the production of, cancer of the breast is borne out by measurement, and by demonstration that the urinary estrogens are often significantly raised in patients with breast cancer.[14,15] Our own experience amply bears this out, "postmenopausal" urinary estrogen values in some of these cases being as high as 4000 I.U. per twenty-four hours (Tzn),* a figure almost forty times that expected. The significance of these remarkable findings cannot be overemphasized. Whatever the mechanism, we seem to have here for the first time an instance wherein a malignant tumor is associated with increase in production of its own growth stimulant.

Ovaries that are the seat of cortical stromal hyperplasia show on macroscopical section a rind of brown-yellow color of increased thickness, and a scalloped surface. On staining with hematoxylin this shows up as a dense blue area. Microscopical examination shows whorls and interlacing fascicles weaving about variable numbers of capillaries and dipping irregularly into the relatively cellular eosinophilic medullary stroma. The cells have enlarged nuclei with abundant coarse granular chromatin, with well defined cell margins and clear intercellular zones.[6,7,9,16]

The Disease in the Male

The prognosis of the disease in the male (whether iatrogenic or spontaneous) is more grave than that in the female. This may be due to the fact that men are not alert to the possibility that they may have this disease. A lump in the breast may go unchallenged for a long period, and spread will have occurred to distant sites before medical advice is sought. The absence of fat in the male breast permits direct extension of the growth to the pectoral fascia and muscles, and this may lead to early lymphatic spread.

Despite these factors, the poor prognosis in this group cannot be explained entirely on anatomic grounds. It seems that these lesions fall into a group in which there is increased "invasive" activity of the malignant cell, and this is shown in the growth,

*This term, and normal values, are defined below in the section entitled "The Study of the Patient."

spread and virulence of the disease. Carcinoma of the breast arising in the male (or in the senile female) appears to have commenced its growth in the relative *absence* of estrogens, as contrasted with the younger female. This may be of interest in relation to the fact that it is in the senile form of the disease in women that one is most apt to achieve favorable results from the *administration* of estrogens.[1,17-20] In the male, by the same token, orchiectomy and estrogen administration may produce amelioration. This is in sharp contrast to the marked aggravation of the disease in younger women occasioned by administration of estrogens, described in greater detail below.

It is of interest that in the past fifteen years a new group in which this disease has developed has been observed. Estrogen therapy in the treatment of men suffering from carcinoma of the prostate is the etiologic factor. Mammary cancer, usually bilateral, has been reported to follow estrogen administration.[21,22]*

Lactation and Nursing

Not only is there an optimum steroid environment for the development of this disease but also there are important local factors that relate to the cyclic achievement of cellular differentiation and lactation. The establishment of lactation and the act of nursing a child reduce the likelihood of later development of cancer of the breast. Numerous statistical surveys of incidence have shown that this disease is commoner in the unmarried than the married woman, and in married women it is commoner in those who are less fertile.[23-26] Nursing mothers have a lesser incidence than those who do not nurse; a nursing period of three to six months appears to be safest from this point of view. Very protracted nursing for periods of one to three years is also hazardous in this regard.[26] Cade,[27] quoting Chase,[21] points out that the Chinese amah, or professional wet nurse, rarely has breast cancer, whereas it is particularly common in the higher social classes, — the Mandarins, — in whom suckling is not practiced.

From the view of cancer prevention and public health, we therefore suspect that *normal pregnancy, lactation* and *nursing* are of prophylactic significance. Obstetricians and pediatricians have a role in this disease of which they may not always be aware.

For reasons of space we have not reviewed here any of the data on the contention that chronic cystic mastitis is of etiologic significance in this disease.

II–The Nature of the Disease

Histologic Types†

Breast cancers are epithelial in origin and arise either from the epithelium of the ducts or acini and hence should be classified as adenocarcinomas. There are four main subdivisions based on distinct histologic patterns. Rarely does a single type appear in the pure form: each is usually accompanied by at least one of the others. All four types may be seen in the same tumor mass. In the initial stages of all types the cells are cuboidal to columnar, but soon the rate of division of the cells, the effect of pressure of the accompanying stroma or the reaction of the host tissue all join to modify this picture so that the cells become round (spheroidal cell), polygonal or even squamous in appearance. The architecture of the tumor also changes. Some tumors maintain their alveolar pattern in a matrix of host stroma, but many others become sheets of infiltrating anaplastic cells in which all relation to the parent tissue is lost.

The four histologic types of this disease are indicated as scirrhous carcinoma (or carcinoma simplex), papillary carcinoma (including the intraductal or comedo carcinoma), medullary carcinoma and mucinous (or colloid) carcinoma, all of which are described in standard textbooks. The future may hold some clue to the biologic or endocrinologic significance of these types; up to the present they have represented a classification of purely morphologic interest.

Since the work of Huggins and Dao[28] on adrenalectomy and the development of their hypothesis that the greater the differentiation of an adenocarcinoma the greater the chance that the tumor is hormone stimulated, renewed interest has been shown in the histologic type of the primary lesion. It is now generally conceded that although the highly differentiated adenocarcinoma is often hormone stimulated, it is by no means always so. Some adenocarcinomas fail to respond to stimulation, and conversely considerable stimulus response is shown by many scirrhous or anaplastic spheroidal-cell tumors. Pearson et al.[29] and many other workers[30-33] have failed to find any distinguishing features in the histologic picture that might be used to differentiate estrogen-stimulated and nonestrogen-stimulated tumors.

Biologic Types

The estrogen-stimulated tumor. The term "estrogen-stimulated tumor" signifies that the tumor responds by increased growth to an increase in level of circulating estrogens. We prefer this to the term "estrogen dependent," which implies that the tumor will not grow without estrogens — sadly, a rare occurrence!

By castrating women with advanced disease, Beatson,[34] in 1896, was able to achieve remissions. Since that time numerous papers[29,33,35-39] have reported beneficial results from oöphorectomy or ovarian irradiation. Others have cited a favorable response to the natural menopause. It is assumed that these tumors are in part stimulated by the estrogens bathing

*This points up a hazard in long-term estrogen treatment of benign or functional gynecologic disorders, postmenopausal osteoporosis or other clinical settings.

†Paget's disease of the nipple is excluded from discussion in this review.

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the cancer cell and that removal of this growth stimulus temporarily results in retardation or regression of the disease.

On the basis of empirical success with oöphorectomy or adrenalectomy it has been estimated that about 40 per cent of tumors arising in younger patients are clearly estrogen stimulated. It should be emphasized that more discriminating measures of endocrine reactions[40] may become available, indicating subtle gradations not evident when "stimulation" or "dependency" is based only on the apparent benefit of endocrine surgery. Current criteria for estrogen stimulation are therefore necessarily ill defined. In our recent experience with the stilbestrol test (described below) we have not encountered any patients in the younger group who did not give some evidence, however slight, of transient worsening indicating a response to estrogen stimulation. We therefore believe that virtually all tumors in the young or menopausal age are "estrogen stimulated": they will grow less well, for a time, with less estrogen.

The pituitary-stimulated tumor. Considerable experimental evidence has been produced that administration to animals of extracts of the pituitary-containing "growth hormone" may cause changes indicating production or stimulation of cancer. Moon et al.,[41] giving growth hormone to intact rats of the Long–Evans strain, after prolonged administration, could induce neoplasms of lymphoid, ovarian and adrenal and mammary tissues. Mirand,[42] in mouse tumors, showed that growth hormone produced an increase in tumor growth.

With the advent of hypophysectomy as a therapeutic measure for advanced disease, a new understanding of the relation between the pituitary gland and mammary cancer is developing. By study of the reported results of women treated by serial oöphorectomy, adrenalectomy and hypophysectomy it will be possible to discern whether or not there is a type of growth stimulated by pituitary activity alone. This has been suggested[43] by the remission obtained in a man who, showing no improvement after orchiectomy and adrenalectomy, did so with hypophysectomy. With the use of the bioassay for mammotrophic hormone[44] the urinary level of this presumably pituitary hormone can be demonstrated to fall after hypophysectomy.

Hormone-independent tumors. In the senile female we have no incontrovertible evidence at present for the existence of a hormone or hormones that stimulate the growth of the tumor. As mentioned above, estrogens may actually inhibit these tumors.

Assessment of the stimulus response of breast tumors at intervals in the course of the disease may demonstrate alterations in the degree of response. A tumor initially demonstrated to be strongly responsive to estrogen withdrawal may, in the course of time, lose this property and ultimately revert to an entirely autonomous growth behavior. Since all patients with metastatic disease ultimately succumb despite endocrine measures currently available, one may tentatively generalize that most, if not all, breast tumors are capable of progressive growth in the absence of ovaries and adrenal and pituitary glands.

Among young women with carcinoma of the breast some (often with rapidly progressive disease) show no apparent benefit from steroid withdrawal even though they may be worsened by estrogens. The question of whether or not such tumors are hormone stimulated becomes an exercise in semantics. Therapeutically, they are beyond the reach of help by endocrine medication or operation.

Types of Spread

This disease will kill 37 out of every 1000 women who die after reaching maturity.[21] The life expectancy of a group of untreated patients with carcinoma of the breast is thirty-nine months.[45]

The disease may spread by direct extension, by lymphatics or by blood stream or by all three. Handley[46] showed that 34 per cent of 119 cases had spread via the internal mammary chain; 60 per cent of the medial lesions had done so. Wyatt et al.[47] stressed the fact that 15 per cent of women with negative axillary lymph nodes had positive internal mammary lymph nodes.

Blood-stream spread leads to involvement of the skeleton and remote viscera. The former is often compatible with long life; the latter (to liver, brain or lungs) is often rapidly lethal. Hepatic metastases are a bad omen for the success of endocrine surgery[31,32]; poor liver function may reduce estrogen inactivation and worsen the disease.[48] Frequent metastasis to the site of production of stimulating hormones (ovaries and adrenal and pituitary glands) is a striking and significant finding in our experience and in that of others.[49]

In the present state of our knowledge we cannot relate *route* of spread to prognosis or treatment. *Sites* of spread are important, the skeleton often being "benign" and the viscera lethal. But *speed* of spread is the all-important factor. The "slow" tumors are those reacting most clearly and favorably to the many endocrine steps now available.

Clinical Types

The endocrine age of the patient, the biologic nature of the tumor, the site of spread and the rate of growth determine the clinical type of the disease. For the approach to the treatment of an individual patient it is most helpful to consider these total circumstances in the host-tumor relation. For ease of description, and with obvious oversimplification, we distinguish eight clinical types of carcinoma of the breast. Classification of the patient into one of these eight large groups is the objective of study as outlined below. It forms the basis for the selection of surgery, hormones and irradiation, as described in

the two final sections of the review. This grouping is basic to our management of the individual patient, as outlined in the last, summarizing section.

In brief, these eight groups are:

A. The Early Lesion without Known Spread in Young or Menopausal Women — "The Young and Early."

B. The Early Lesion without Known Spread in the Senile Woman — "The Old and Early."

C. Limited Local Disease with Slow Spread to the Soft Tissues in Young or Menopausal Women — "Slow, No Bones."

D. Rapid Spread of the Local Disease — "Fulminating."

E. Late Stage Disease with Involvement of Lungs, Liver and/or Brain — "Late Visceral."

F. Slow Progression with Skeletal Metastases — "Slow with Bones."

G. In Pregnancy.

H. The Male.

III–The Study of the Patient

As each patient appears for treatment, the surgeon should try to place her clinical type and then answer six further questions, as follows:

Where is the patient in the natural course of her disease?

Does breast surgery have anything to offer?

Is the tumor stimulated in its growth by any hormones?

If so, where are such hormones being generated in the body?

Can withdrawal of these by surgery, or administration of hormones medicinally, affect the tumor favorably?

Can irradiation help?

These questions are answered by a systematic course of study starting with the history and physical examination.

Clinical Examination

History and physical examination. In a review of this type, there is not space to detail the many features of the surgeon's initial examination that will be critical in his plans for treatment. Despite the growth of many new laboratory methods, this clinical examination remains the most important. The extent of spread, the rate of spread, the effect of the disease on the patient's health, morale and insight and, most important, the orientation of the patient in the time progress of her disease will all be based on a thorough history and physical examination.

In many previous accounts the formal "stages" of the disease have been defined. A simplified form of Portmann's[50] classification follows:

Stage 1. Tumor confined to the breast itself.

Stage 2. Tumor in the breast with skin attachment or palpable axillary glands or both.

Stage 3. Stage 2 and/or supraclavicular or contralateral axillary glands or fixation to the pectoral fascia.

Stage 4. Visceral or skeletal metastases.

The formal stage of the disease should be noted and recorded.

In local examination of the patient who has had previous mastectomy particular attention should be given to the adequacy of the operation: are the pectoral muscles or their axillary portions still in place? If so, an axillary dissection cannot have been extensive.

Laboratory Procedures

X-ray examination. The patient may have a long illness ahead. Economy in the use of x-ray examinations and intelligent spacing of serial studies will be appreciated. Initially, films of the chest, spine and pelvis will disclose most pulmonary or skeletal lesions. These, as well as films of areas of pain, are sufficient to start with. When bone disease is demonstrated one rarely gains anything by repetition of films oftener than once in eight to ten weeks under active treatment.

Endocrine assays.

Follicle-stimulating hormone (FSH.) In all women near or after the menopause or in whom x-ray "castration" has been carried out, a urinary FSH determination should be performed. The technic of Klinefelter et al.[51] is suggested. A twenty-four-hour aliquot of urine is needed. If the result is in the normal range below 50 mouse units per twenty-four hours on two determinations, the patient may be assumed to have significant estrogen production. If elevated, above 100 mouse units per twenty-four hours, estrogen production is unlikely to be of significance.

Estrogens. In all patients with advanced disease at or after the menopause or castration, these data are vital to intelligent treatment. In women in the reproductive age they are of less value until the patient has been castrated. If x-ray "castration" has been carried out, the test is a prerequisite to the selection of further treatment.

Measurement of urinary estrogens is not an easy procedure, and although technics have been developed using fluorimetry, chromatography or countercurrent distribution, they have failed to provide information of clinical significance in this disease. We have used the Smith and Smith[52] technic of hydrolysis, extraction and bioassay.

Two values of clinical significance can be obtained and measured in this assay. A fifteen-minute hydrolysis with concentrated hydrochloride will deconjugate estradiol, estrone and estriol, those biologically

active estrogens excreted normally in the conjugated (inactive) form. This is known as the "To" activity. A second fraction is also prepared in which, after a three-hour hydrolysis with concentrated hydrochloride and zinc, a further yield of free estrogen is obtained and can be measured. This activity is known as "Tzn" and is derived at least in part from steroids other than estradiol, estrone and estriol, which are converted by the hydrolysis into the highly active estradiol.

Thus, by assaying these two fractions, it is possible to gauge the excretion of ovarian estrogens and also of related steroids. As applied to the study of mammary cancer in castrated or postmenopausal women, the results of Smith and Emerson[15] point to the adrenal glands as the principal source of the very high Tzn activity observed by them in such subjects (Table 1). No definite values can be given for postmenopausal women with ovarian cortical stromal hyperplasia. High levels are common but not invariable. In postmenopausal patients with cancer of the breast, estrogen activity (To) in the range of 50 to 125 I.U. per twenty-four hours may be observed, with Tzn values as high as 5000 I. U. per twenty-four hours.

Mammotrophin. Scowen and Hadfield[44] have described a test for nonovarian mammotrophins. This is a bioassay based on urine. It may become a test of value particularly in selecting patients for hypophysectomy, since the active principle is presumably pituitary in origin. We have had no experience with it.

Blood and urine steroids and eosinophil counts. These studies are useful when adrenal inhibition is under study. Any of the commonly used technics[63] will help one judge adrenal inhibition or the completeness of adrenalectomy.

Metabolic and chemical studies.

Studies of the blood. In addition to the complete blood count, certain studies are useful. The electrolyte and protein profile (blood urea nitrogen, carbon dioxide, chloride, sodium, potassium and protein) provides an index of the general health of the patient and is useful in evaluating "lateness" of the disease. The serum calcium concentration provides a more sensitive index of activity of this disease than does the phosphorus. Elevation of the serum calcium over 5.8 milliequiv. per liter (11.6 mg. per 100 ml.) is highly suggestive of rapid growth of the bone lesions. Alkaline phosphatase may be elevated in the presence of bony metastases and show an increase either on aggravation or shortly after amelioration of the bone involvement. A certain fraction of the acid phosphatase[54,55] may show significant elevations with extensive soft-tissue lesions and in the presence of bone disease. Extensive hepatic metastases may be associated with a rise in serum alkaline phosphatase, with or without biliary obstruction.

Calcium excretion studies. Pearson and his group[56,57] at the Memorial Hospital were the first to appreciate the fact that the alterations in urine calcium excretion seen in patients with osseous metastases might be used to assess the rate of progress of the disease and its hormonal reactions. Metastatic tissue will replace bone matrix volume for volume and it can be estimated that when 1 gm. of bone is replaced, approximately 100 mg. of calcium is excreted in the urine.

To carry out this study, a diet containing a maximum intake of 200 mg. of calcium per day is started. After a three-day period (during which calcium excretion stabilizes) twenty-four-hour urine collections are begun, and calcium determinations made. A normal woman on such a diet will excrete between 50 and 100 mg. per day,[6,58] but a woman with osteolytic metastases will excrete from 200 to 1000 mg. of calcium, the exact figure varying according to the mass, activity and rate of growth of the deposits.

TABLE 1. *Normal Values for Urinary Estrogens.*

SUBJECT	TO VALUE	TZN VALUE
	I.U./24 hr.	*I.U./24 hr.*
Young women*	20-900	50-700
Normal postmenopausal women	25-50	50-100

*Range large, owing to change in levels of cycle.

This form of study can be used for two main purposes:

The rate of growth of the disease may be measured at intervals. Short-term calcium studies (of three or four days) under standard resting conditions repeated at intervals of several months may show changes in the rate of calcium excretion. A rise in successive tests indicates increasing mass and activity of the disease and a fall a diminishing rate of growth.

Hormone stimulation and selection of endocrine treatment may be studied. Many workers[17,29,59-66] have noted that changes in urine calcium excretion and serum calcium levels accompany the changing hormone levels seen in the menstrual cycle of patients with osseous metastases and have observed similar changes in patients under treatment with estrogen or testosterone propionate.

The stilbestrol stimulation test. To carry out this test, 10 mg. of stilbestrol is administered by mouth daily for three days, and the results are assessed in two ways, — chemical and clinical, — both of which we believe to be of importance.

A rise in urine calcium excretion, serum calcium concentration or both. This change is only observable in patients with skeletal metastases. The excretory change may be prolonged, occasionally lasting three or four weeks before returning to the prestimulation level. The increased urine calcium excretion usually appears within a day or two of the last dose of stilbestrol but may be delayed for several days. If sufficient bone destruction occurs, the mobilization of calcium may be great enough to exceed the renal clearance, and hypercalcemia will develop. This will be found when the excretion of calcium exceeds 500 mg. per day[6] or at lower levels in the presence of renal insufficiency.

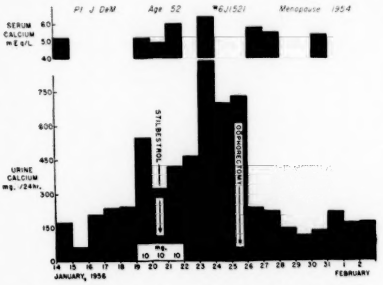

FIGURE 1. *Course in an Endocrinologically "Young" Woman of Fifty-two with Carcinoma of the Breast and Skeletal Metastases, Showing, by an Increase in Urine and Serum Calcium, a Positive Stimulation of the Disease by Stilbestrol. After oöphorectomy there is a decrease in urine calcium excretion to, but not below, the prestimulation level. Slight clinical aggravation of bone pain occurred on stilbestrol.*

This test is of value when a clear-cut rise in urine calcium excretion is seen *or* when no change in levels whatsoever occurs. Experience is essential in interpretation of the result. With any bone disease a clear increase (over 50 per cent) means that hormone stimulation has occurred. Only with widespread bone disease can lack of change be interpreted as indicating lack of estrogen stimulation.

The systemic response. Increase in bone pain, malaise, pyrexia, nausea and vomiting indicate a positive response: hormonal stimulation of the tumor. These observations may be made with soft-tissue as well as skeletal disease. The clinical and chemical changes subside when the drug is stopped.

It should be stressed that this test may produce complications. The patient's condition should be assessed daily. Any evidence of severe systemic manifestations, hypercalcemia or renal failure should terminate the procedure; complications are rare when hypercalcemia and hypercalcinuria are not present.

Many factors other than the growth or regression of skeletal tumor may alter urine calcium excretion. Alterations in absorption, the degree of immobilization, pathologic fractures, hormone-induced osteogenesis (estrogen, androgen) or osteoporosis (cortisone) or surgical operation itself must all be considered. Adequate control equilibration, constancy of condition and the nature of the response help in interpretation. Estrogen administration in the menopausal woman might be expected to reduce urine calcium excretion (and cortisone to increase it), and it is the reverse of this that occurs in the stimulated tumor. Of a group of 5 control patients without cancer whose calcium excretion was studied after other operations, all showed a transient decrease in urine calcium excretion, none lasting more than five days.

This test should never be done in the presence of pre-existing hypercalcemia or when the daily urine calcium excretion is 300 mg. or more on a 200-mg. calcium diet, or in the presence of diminished renal function.

The following case illustrates the type of calcium excretion that may be observed in the response to stilbestrol stimulation:

J.D. (P.B.B.H. 6J152), a 52-year-old woman, had a radical mastectomy on the right for carcinoma in August, 1948. She remained well until September, 1955, when bone pain developed and osseous metastases were demonstrated.

She had borne 5 children; all were breast fed for 6 or 7 months. She had had a normal menopause at the age of 50.

She was admitted to the Peter Bent Brigham Hospital in January, 1956, and on examination her general condition was found to be good. The only evidence of recurrent soft-tissue disease was a clinically malignant lymph node in the right supraclavicular fossa.

X-ray study showed extensive osteolytic bone lesions. The serum calcium was 5.2 milliequiv. per liter, and urine calcium 170 to 200 mg. per twenty-four hours on a low-calcium diet.

A stilbestrol stimulation test was carried out, and a marked response obtained. Nausea, emesis and increase in bone pain were associated with hypercalcemia and hypercalcinuria. Although the patient was postmenopausal at this time, the tumor was still potentially estrogen stimulated. Initial attention must be devoted to the ovaries as a site of continued stimulation (Fig. 1).

The cortisone-inhibition test. Patients who relapse after castration may do so because of the stimulus of a raised level of circulating estrogens of adrenal origin. If the tumors are hormone stimulated a further remission may be achieved by adrenalectomy or hypophysectomy. Selection of these cases may be aided by suppression of adrenal function with cortisone and observation of the urine calcium excretion.

In the study of adrenal inhibition a quantitative approach is possible by a combination of calcium studies with the measurement of the urinary (Tzn) estrogens under cortisone therapy. Or the urine 17-hydroxycorticoids may be measured during treatment with fluorohydrocortisone.[67]

On the basis of studies[15] showing decreased estrogen production (both To and Tzn) in the castrated woman treated with cortisone, it is clear that "crossed

inhibition" does occur and that cortisone administration will decrease estrogen production.

The study of the calcium response to the administration of growth hormone or other pituitary fractions may become of value in selection of patients for hypophysectomy. Experience is still insufficient, and conclusions uncertain.

Having considered the examination, roentgen and endocrine study of the patient, we may now pass on to a consideration of available treatment: breast surgery, endocrine medication or surgery, and irradiation. These will be reviewed briefly in the next three sections.

(To be continued)

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MEDICAL INTELLIGENCE

URINARY-TRACT MALFORMATIONS*

Their Familial Occurrence, with Special Reference to Double Ureter, Double Pelvis and Double Kidney

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PHILADELPHIA

IN the past twenty years little mention has been made in the American literature of the familial occurrence of urinary-tract malformations. Reports on cases of double kidney, pelvis and ureter in families are rare and confined entirely to foreign publications.[1-4]

Because the literature on this subject is scanty and the relation is probably much more common than has previously been known, it was thought advisable to publish our observations of upper-urinary-tract duplication involving 3 of 4 members of a family.

CASE REPORTS

CASE 1. N.T., a 5-year-old girl, was admitted to the hospital on February 2, 1953, with complaints of fever and bilateral costovertebral-angle pain of 1 week's duration. For the past year she had had repeated urinary-tract infections, and she had always shown poor weight gain. The parents' marriage was not consanguineous, and there was no known history of familial urinary-tract anomalies or disease.

Physical examination, which showed a thin, pale girl who weighed 15 kg. (33 pounds), was not remarkable.

The temperature was 100°F., and the pulse 120. The blood pressure was normal. There was a mild anemia. Urinalyses consistently revealed albuminuria and pyuria. Bacteriologic study of the urine repeatedly demonstrated *Escherichia coli*. Renal-function studies were negative.

Intravenous and retrograde pyelography revealed complete ureteral duplication on the right, the superior pelvis being a large, multiloculated, hydronephrotic sac with a greatly dilated ureter. The ureter for the inferior pelvis was moderately dilated. The left ureter was dilated in its distal ⅓, and fullness of the left pelvis was seen. The diagnosis of right-sided ureterocele was confirmed by cystoscopy.

Operative procedures consisted of excision of the ureterocele and resection of the upper hydronephrotic portion of the right kidney. At operation separate blood supplies were demonstrated to both halves of the right kidney.

The postoperative course was stormy and prolonged as a result of repeated urinary-tract infections, which eventually responded to appropriate antibiotic therapy and catheter drainage.

The patient did well after discharge on June 21, and intravenous urography on follow-up study revealed normal findings on the right, with minimal hydronephrosis on the left.

CASE 2. D.T., a 3-year-old girl, was admitted to the hospital on March 31, 1953, with a limp of 2 weeks' duration unassociated with pain or fever. She had gained weight poorly and had repeated bouts of abdominal pain, fever and headache.

Physical examination showed a thin girl, who weighed 10.4 kg. (23 pounds). Complete physical and neurologic examinations were negative except for the slight limp, which disappeared in 3 days.

The temperature was 98.6°F., and the pulse 120. The blood pressure was normal.

There was a mild anemia. Daily urinalyses and repeated bacteriologic examinations of the urine were negative, as were renal, hepatic and agglutination studies. X-ray films of the chest, spine, hips and long bones were normal.

In view of the history of repeated bouts of fever coupled with the knowledge of urinary-tract duplication and disease in the patient's sister, intravenous urography was performed, revealing right incomplete double ureter, pelvis and kidney, with no evidence of obstructive uropathy.

TABLE 1. *Occurrence of Urinary-Tract Duplications in Family T.*

MEMBER OF FAMILY	AGE	DESCRIPTION OF DUPLICATION
	yr.	
Mother (G.T.)	28	Unilateral (left), incomplete (or bifid) double ureter, pelvis & kidney
Father*	?	?
Daughter (D.T.)	3	Unilateral (right), incomplete (or bifid) double ureter, pelvis & kidney
Daughter (N.T.)	5	Unilateral (right), complete double ureter, pelvis & kidney

*Separated from family & could not be located.

CASE 3. G.T., the 28-year-old mother of Cases 1 and 2, was a small, thin woman who had no urinary complaints. In view of the presence of upper-urinary-tract duplication in her children, intravenous pyelography was performed, which revealed left incomplete unilateral double ureter, pelvis and kidney, without evidence of obstructive uropathy.

The foregoing cases represent Family T. (Table 1), which is added as a sixth family to the 5 previously reported examples of familial duplication of the upper urinary tract, confined to the foreign literature.

DISCUSSION

Although it is well known that congenital anomalies frequently occur in brothers and sisters, little mention is made of this fact in relation to certain malformations of the urinary tract. Probably the best recognized form of urologic anomaly that shows a strong familial hereditary tendency is polycystic disease.[3,5-7] In the laboratory animal[8-10] various urinary-tract malformations such as renal agenesis, hypoplasia and atresia of the ureter have been shown to be hereditary. The familial occurrence of renal agenesis has also been observed in human patients.[11-13]

Although ureteral duplication with double renal pelves occurs more often than all other urinary-tract malformations, its familial occurrence has not been stressed. To date, only 5 familial cases of double kidney, pelvis and ureter have been documented, and these have been in foreign publications.

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Ritter[1] reported a family in which 4 of 12 members studied had double ureters; these were 2 sons, a daughter and her son in turn. Steinlin[4] described 2 sisters and a brother with ureteral duplication; subsequently, he surveyed families in which double ureters occurred and discovered another familial case with double ureter in a sister and brother. Kares[2] presented the cases of 2 brothers with ureteral duplication. Frissel's[3] report, in 1942, of 2 sisters with double ureter is the latest.

Interestingly enough, in the 5 previously reported families no information is available concerning the parents of the last 3 cited, and the first 2 families had only negative information concerning 1 parent. In Ritter's[1] report, however, 1 affected daughter in turn had a family in which 1 child also possessed a defect of upper urinary-tract duplication. This case and the family described above seem to be the only cases reported with positive information on at least 1 parent.

In the family presented in this article, upper-urinary-tract duplications were detected in 3 of 4 members available for study. One daughter showed unilateral, right-sided, incomplete double ureter, pelvis and kidney; the other had unilateral, right-sided, complete double ureter, pelvis and kidney. The mother had left-sided, unilateral, incomplete double ureter, pelvis, and kidney.

From the data available, familial duplication of the upper urinary tract appears to affect males and females equally. In contrast, such anomalies of the lower urinary tract have no reported familial occurrence.

Recognition of the familial occurrence of double ureter, pelvis and kidney becomes of some importance when one realizes that duplication of the upper urinary tract is the most common urinary-tract anomaly,[3,14] occurring in almost 1 per cent of the population.[7,15,16] Furthermore, since this anomalous organ is twenty times more prone to pathologic complications than a normal kidney,[17] because of frequently associated obstructive defects, its detection would permit early surgical correction long before complications of hydronephrosis, infection and calculi destroyed renal tissue and then finally — and possibly — produced symptoms. It becomes apparent, therefore, that once duplication of the upper urinary tract is discovered in a patient, all members of that family warrant intravenous pyelography. Such an approach not only will help establish the true familial distribution of this anomaly but also may avoid unnecessary and hitherto unknown renal damage.

Summary and Conclusions

Three cases of upper-urinary-tract duplication occurring in a single family are presented.

In all probability familial occurrence of double ureter and kidney occurs much more frequently than the available literature indicates.

In cases in which such duplications exist, intravenous urography on all members of the family may be warranted.

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DOCTORS AFIELD

Jean Baptiste Charcot — Physician, Explorer, Oceanographer

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THROUGH the years, many physicians have left the practice of medicine to seek fame and fortune in other fields. Some have attained prominence and distinction in politics, philosophy or letters. Few, however, have established a reputation in the field of polar exploration. One such physician who abandoned medicine to devote his life to the exploration of polar areas was Jean Baptiste Auguste Étienne Charcot.

Born at Neuilly-sur-Seine near Paris on July 15, 1867, Jean Baptiste was the son of the illustrious French neurologist, Jean Martin Charcot. From his earliest years, young Charcot was attracted and fascinated by the sea. His intentions were to enter "l'École navale." However, this did not meet with parental approbation. The father was most desirous that his only son follow in his footsteps. And so, Jean Baptiste studied medicine; nevertheless, he retained his interest in ships and his love for the seas.

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In 1891, he served an internship at La Salpêtrière, and during that period he took advantage of every opportunity to sail at Argenteuil on the Seine. In the following year, he served under Dr. Edouard Brissaud at the hospital Saint Antoine. The year 1893 marked the death of the elder Charcot. Jean Baptiste continued in the field of medicine and by 1895 had become "chef de clinique" under Dr. Fulgence Raymond at Saint Antoine. Later, he spent three years in cancer research at the Pasteur Institute. Together with his associates, he had presented papers of considerable merit and seemed destined for even greater success. At this stage, he was greatly influenced by a revival of interest in polar explorations, and although trained for the medical profession, he decided to cast his lot with the sea. Henceforth, he attained his triumphs no longer on hospital wards but in polar areas, facing the perils of the sea, wind, ice and bitter cold.

For a time, he worked in a maritime research laboratory. Then, in 1902, he conducted his first expedition to the Faroe Islands, the Hebrides and Jan Mayen Land. In the following year, he set sail aboard the *Français*, in search of the missing polar expedition of Otto Nodenskjold. Scarcely had he reached South America when he heard of the expedition's rescue. He pushed on and explored the west coast of Graham Land, discovered Loubet Coast and sighted Alexander I Land. During this expedition, which lasted until 1905, Charcot and his staff acquired large collections of geologic and zoologic specimens and amassed precise scientific data on those areas.

From 1908-1910, Charcot conducted his most important expedition. Aboard the polar yacht *Pourquoi Pas?*, built according to his specifications, he mapped the coast of Graham Land and discovered Adelaide Island, Marguerite Bay and Charcot Land, which he named in honor of his father. In recognition of his outstanding scientific work, the French Geographic Society awarded him its gold medal in 1912.

When World War I broke out, Charcot was a reserve officer. He was called to active duty with the medical service. However, thanks to the intervention of the British Admiralty, he was able to transfer out. Placed in command of an auxiliary ship, *Le Meg*, he engaged in submarine hunting off the coast of west Scotland throughout the war.

At the close of the war he resumed his explorations. In 1921, he visited Rockall, a remote island located between Iceland and Ireland. In 1925 he searched for the polar explorers Amundsen and Guilbaud, exploring the Greenland coast once more. In 1928, he searched for the wreck of the *Latham 47*. Annual expeditions along the Greenland coast followed. He conducted several trips to Scoresby Sound in 1931, first selecting a site for a French observation station and then transporting a group of scientists to and from the Sound.

On May 5, 1931, Charcot read a paper before the Academy of Medicine in Paris, describing a disease, resulting from the prolonged ingestion of canned foods, that he had observed during polar hibernations. This clinical entity later became known in French colonial areas as Charcot's disease. It was evident that he had not lost all interest in medicine although he had turned to the field of exploration.

It was somewhat ironical that he perished during the last voyage that he had decided to make. After a trip to Copenhagen, the *Pourquoi Pas?* was lost at sea on September 15, 1936. Caught in a heavy gale off the coast of Iceland, the ship sank after a violent explosion. A lone crew member, the quartermaster, survived this shipwreck. He gave a vivid account of the last moments of this gallant ship and described Charcot standing on the bridge to the very last. All bodies were recovered except one. The naval transport *Aude* brought back the bodies of Charcot and his crew to the port of Saint Malo. In Paris, a solemn state funeral was held in the cathedral of Notre-Dame.

During his lifetime, Charcot received the highest honors. He held membership and gold medals from all the major geographic societies of the world. He was admitted to the academies of medicine, marine and science and made a grand officer of the Legion of Honor.

Physician, explorer of polar regions and uncharted seas for almost three decades, Charcot truly dedicated his life to scientific research. His entire career was certainly in the finest tradition of the great men of France.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42181

PRESENTATION OF CASE

A forty-year-old housewife entered the hospital because of enlarged cervical lymph nodes.

Beginning twenty years previously there were four episodes at yearly intervals of painless swelling of cervical lymph nodes on the right side of the neck. During the first episode there was drainage of pus for two weeks. In the next year several teeth were extracted, and a superficial abscess just below the angle of the right side of the mandible was incised and drained. The patient treated herself with poultices during the next two episodes when pus also drained. No further lymphadenopathy was noted until about a year before admission, when a small lump that subsequently varied in size appeared below the anterior portion of the mandible. Six months before entry several swellings were noted over the right side of the neck. None of the earlier episodes or recent enlargements of the cervical lymph nodes were associated with fever, chills, sweating or weight loss.

A sister had died of tuberculosis six years previously. An x-ray film of the chest three years before admission was said to have been normal. Six years before entry there was an episode of syncope associated with palpitation of the heart, blurring of vision for ten days and unsteadiness of gait for two months. There was complete recovery. At the age of twenty there was an episode of pain, swelling and stiffness of the right wrist and fingers. A cardiac murmur was said to have been audible subsequently. Three years later there was an episode of pain in the right hip. For six years before admission dyspnea was noted after climbing one flight of stairs. One month before entry there was an episode of iridocyclitis.

Physical examination revealed a well nourished woman of athletic physique. The right pupil was larger than the left, and there was a precipitate on the right cornea. There was no lid lag. Examination of the fundi showed Grade 1 hypertensive changes. There were enlarged, nontender, movable cervical and submandibular lymph nodes measuring up to 3 cm. in diameter on the right side of the neck. In the right lobe of the thyroid gland there was a firm, nontender nodule measuring 3.5 cm. in diameter. The heart was not enlarged. The aortic second sound was greater than the pulmonic. A Grade 1 aortic systolic murmur was audible. Examination of the abdomen was negative.

The temperature was 98.4°F., the pulse 80, and the respirations 18. The blood pressure was 220 systolic, 120 diastolic.

The urine was normal. Examination of the blood showed a hemoglobin of 11.6 gm. per 100 ml. and a white-cell count of 9400. The serum nonprotein nitrogen was 17 mg., the total protein 8.1 gm., the albumin 4.9 gm., the globulin 3.2 gm., and the fasting blood sugar 82 mg. per 100 ml. The radioactive-iodine uptake was 38.4 per cent in twenty-four hours. The basal metabolic rate was −17 per cent. X-ray films of the chest demonstrated some extrinsic pressure on the right lateral aspect of the trachea in the region of the thyroid gland. There was no evidence of calcified lymph nodes in the neck or calcification in the thyroid gland. Fluoroscopically, the barium-filled esophagus appeared normal; the heart and lungs were normal. An intravenous pyelogram was negative. An electrocardiogram showed changes compatible with left ventricular hypertrophy.

On the seventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. THOMAS J. ANGLEM*: Is there anything further to be said about the x-ray films?

DR. JOSEPH HANELIN: One finding, which was not mentioned in the protocol and may not be important, is the calcification lying above the left kidney, possibly in the adrenal gland. The pyelogram is normal. The heart is not enlarged although there may be some increased rounding of the contour of the left ventricle. There is pressure upon the lower portion of the trachea in the neck, probably the result of enlargement of the thyroid gland.

DR. ANGLEM: The first problem to be decided is whether or not the original episode twenty years before admission was a tuberculous or a nonspecific lymphadenitis. In none of the episodes did the patient have fever, chills or any evidence of a reaction that one would expect with a nonspecific infection. The fact that this relatively chronic process recurred repeatedly over a four-year period is more suggestive of a tuberculous lymphadenitis than of a nonspecific lymphadenitis. The suppuration rules out most of the other causes of lymphadenitis that are usually mentioned in a differential diagnosis. The second

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problem is to decide whether or not the lymphadenitis present at the time of admission was related to the early episodes of lymphadenitis or whether it was an independent, new disease. Characteristically, tuberculous lymphadenitis exhibits periods of remission, with exacerbation, that may last for sixteen years or even longer.

The second diagnosis that must seriously be considered is carcinoma of the thyroid gland, with metastases to the cervical lymph nodes. Since there was no suppuration associated with the later lymphadenitis, one must raise the possibility of Hodgkin's disease or lymphosarcoma. However, the patient had none of the other findings usually noted with either of those two diseases, such as splenomegaly or a systemic reaction. I think, therefore, that it is unlikely that either one need be seriously considered.

The differential diagnosis, it seems to me, rests between tuberculous lymphadenitis with an unrelated mass in the thyroid gland, probably a multiple colloid adenomatous lobe, and carcinoma of the thyroid gland with metastases to the cervical lymph nodes. Superficially, there seems to be a strong case for carcinoma of the thyroid gland, but as one analyzes it, it becomes less strong. The mass in the gland was reported as firm rather than hard. Most thyroid carcinomas that attain the size of 3.5 cm. are hard in consistence. Moreover, carcinoma of the thyroid gland, with possibly metastatic disease in the lymph nodes of the neck, is difficult to reconcile with the history. The lymph node noted one year before admission was in the submandibular region near the anterior portion of the mandible. Although involvement of submandibular lymph nodes from carcinoma of the thyroid gland does occur, it is uncommon. It is even less common as the first manifestation of carcinoma of the thyroid gland. Furthermore, we are told that the size of this lymph node varied; that would be an unlikely occurrence in a lymph node containing metastases secondary to carcinoma of the thyroid gland. No detailed information was given regarding the position of the enlarged lymph nodes of the neck that appeared six months later.

The case for tuberculous lymphadenitis is considerably stronger. To begin with, the entire history fits together properly. It is not at all unusual for tuberculous lymphadenitis to exhibit periods of quiescence and exacerbations over many years. The chronic, recurring suppuration in the early part of the history is typical of tuberculous lymphadenitis. Moreover, there was probably exposure to tuberculosis. A sister was said to have died of tuberculosis six years before admission, but it is not stated whether the patient was exposed to this infection. One month before entry the patient had an iridocyclitis with features that are usually said to be associated with the tuberculous form of iridocyclitis. The fact that the x-ray films of the chest were normal does not rule out tuberculous lymphadenitis, which commonly exists without coexistent pulmonary disease or at least without disease recognizable on the x-ray film.

The additional data about the thyroid gland — the basal metabolic rate and radioactive-iodine uptake, which was in the euthyroid range — do not give me any help in the diagnosis. It seems to me that this patient had two diseases, a nonmalignant lesion of the thyroid gland, which was probably a multiple colloid adenomatous lobe, and tuberculous lymphadenopathy in the neck.

DR. AUSTIN L. VICKERY: Dr. Taylor, have you a comment?

DR. GRANTLEY W. TAYLOR: I agree with Dr. Anglem. The location of the involved lymph nodes high in the neck is against metastases from a thyroid carcinoma, which may involve higher submaxillary and submandibular lymph nodes only during a later stage.

DR. VICKERY: As the protocol stipulated, some enlarged lymph nodes were submandibular, but others were designated only as cervical.

DR. TAYLOR: I think that the earliest involved lymph node was high up in the neck. I wondered whether Dr. Anglem considered the cardiac status. Were the hypertension and left ventricular hypertrophy relevant or were they incidental findings, perhaps secondary to rheumatic disease?

DR. ANGLEM: I assumed that the patient had recognized hypertension and probably hypertensive heart disease, which had no bearing on the main problem.

DR. REED HARWOOD: Would you say that the fact that the lymph nodes were described as nontender and multiple is against an inflammatory process such as tuberculosis?

DR. ANGLEM: More often than not tuberculous lymph nodes are nontender and exhibit varied degrees of mobility. Sometimes, those in the neck that have been subjected to long-standing disease become matted together, but in the early stages they are usually quite movable.

DR. HARWOOD: What is the significance of the elevated serum protein?

DR. ANGLEM: I do not know how to explain it, nor do I know that it has any significance. I cannot tie it up with either of the diseases that seem to me to represent the possible diagnoses.

DR. JACOB LERMAN: Any infection may increase the globulin.

DR. VICKERY: I saw this patient at Surgical Grand Rounds; Dr. Taylor was also there. I raised the question at the time whether or not a person with an episode of scrofula with drainage twenty years previously could have had smoldering disease for that length of time. I was promptly enlightened by a member of the audience associated with a tuberculosis sanatorium who stated that he had recently seen a woman in her eighties with recurrent tuberculous cervical lymphadenitis who had had tubercu-

losis with neck drainage in her youth. The possibility of tuberculosis, therefore, was certainly one to be considered. Preoperatively, it was thought that the nature of the sizable lateral nodules in the right side of the neck could be tuberculous. It was planned to explore the thyroid gland on that side and to biopsy an enlarged lymph node.

Clinical Diagnoses

? Tuberculous lymphadenitis.
Thyroid adenoma.
Hypertension.

Dr. Thomas J. Anglem's Diagnoses

Tuberculous lymphadenitis.
Multiple colloid adenomatous goiter.

Anatomical Diagnosis

Follicular adenocarcinoma of thyroid gland, with metastases to cervical lymph nodes (probably of twenty years' duration).

Pathological Discussion

Dr. Vickery: At operation a 2-cm. hemorrhagic cystic nodule was found in the lower pole of the right thyroid lobe. A large (2 cm.), soft lymph node in the right posterior triangle of the neck was excised, and a total thyroidectomy performed on the right. Histologically, the lymph node was somewhat of a surprise, for it was totally replaced with a well differentiated follicular adenocarcinoma, clearly identifiable as thyroid in origin. Interestingly enough, the clinically palpable cystic nodule in the thyroid gland proved to be a benign colloid adenoma with old hemorrhage and fibrosis of its wall. However, there were two 1-cm., firm nodules within the thyroid lobe, which were ill defined and not encapsulated and microscopically showed low-grade adenocarcinoma. Other sections of the gland revealed numerous scattered microscopic foci of carcinoma in otherwise normal tissue.

A week later a radical lymph-node dissection of the right side of the neck was done; 8 of 39 lymph nodes, some of which were as large as 3 cm. in diameter, contained metastatic carcinoma. In many areas of the involved lymph nodes, the tumor was so well differentiated with normal-appearing colloid-filled acini that it was virtually impossible to recognize its malignant character by usual histologic criteria. Although papillary adenocarcinomas are, by far, the most common type of thyroid malignant process that metastasizes slowly to regional lymph nodes, no foci of papillarity were found.

The difficult problem that Dr. Anglem discussed is to reconcile the peculiar remote history of drainage from the neck with the eventual finding of thyroid carcinoma. We found no evidence of past inflammation in any of the cervical lymph nodes and as a consequence must assume that if tuberculosis had once been present it had disappeared.

If one were dealing with an organ other than the thyroid gland, it would be presumptuous to claim on the basis of lymphadenopathy of many years' duration with the subsequent discovery of metastatic carcinoma that the carcinoma had been present during the entire period of the known lymphadenopathy. However, some thyroid tumors are notorious for slow growth, late metastases and regional localization over long periods. The literature gives numerous accounts of proved cases of thyroid carcinoma that remained within the confines of the neck — some within the gland and local tissues or in lymph nodes — for many years. To make the statement that this patient had thyroid carcinoma from the time that she first had the lymphadenopathy is going beyond the evidence, but it is a tenable explanation. Survey films of the chest and bones have shown no evidence of further spread of the disease. I think it is likely that the hypertension, rather than the thyroid carcinoma, will be the ultimate cause of this patient's death.

Dr. Anglem: Do you think that the original enlarged lymph nodes were carcinomatous and that they disappeared and then reappeared?

Dr. Vickery: That is a moot question because there is some doubt about whether or not she had enlarged lymph nodes all the time and then suddenly became aware of one that was larger than the others. I cannot be sure of that. We checked the previous hospital admission when the neck drainage was done, sixteen years before this admission, but no tissue was removed; so unfortunately we cannot settle that question.

A Physician: Was a tuberculin skin test ever done?

Dr. Vickery: It was done and was reported as mildly positive at 1:100,000 dilution.

Dr. Taylor: Dr. Hanelin, the absence of calcification in the neck after twenty years is a strong argument against tuberculosis, is it not?

Dr. Hanelin: One would expect calcification. I have not seen enough of these cases to be positive about that. We do have some evidence of tuberculosis other than the positive skin test. There is some calcification of the left adrenal gland.

CASE 42182

Presentation of Case

A twenty-four-year-old chemist entered the hospital because of "pressure" in the chest.

Two and a half years previously he had had three grand-mal seizures in two days. The seizures were preceded by nausea, and there was postictal confusion with retrograde amnesia for two days. With

Dilantin, 300 mg. daily, and phenobarbital therapy he remained well until a year later, when, after rapidly climbing three flights of stairs, he had an episode of syncope lasting for ten minutes. Upon recovery the pulse was noted to be normal. A similar episode occurred several months later after he had been running on a hot day. Stertorous breathing was noted, but there was no convulsion. Shortly thereafter, while mowing a lawn, he noted palpitation and dyspnea as well as aching in the precordium, neck and both arms. This attack stopped abruptly after twenty minutes; the pulse was regular at a rate of 80. Subsequently, several similar attacks, associated with less exertion, occurred. An electroencephalogram was normal. Two electrocardiograms were said to have shown questionable right-bundle-branch block, with T-wave changes. Seven months before admission, while playing basketball, he had a generalized tonic and clonic convulsion, with urinary incontinence. The convulsion was preceded by a feeling of dizziness. Upon recovery he was drowsy but responsive. There was no retrograde amnesia. Physical examination was negative, as was a blood Hinton test. The Dilantin dosage was increased to 400 mg. daily. Two months later there was an episode of palpitation, with weakness, nausea and vomiting and with loss of consciousness for about five minutes. Six similar episodes occurred during the five months before entry. An electrocardiogram during one of these episodes showed ventricular tachycardia that spontaneously reverted to a normal rhythm at a normal rate. An electroencephalogram was normal. Five months before admission an electrocardiogram showed a normal sinus rhythm at a rate of 75; the PR and QRS intervals were 0.19 and 0.10 second, respectively; the P waves were slightly prominent, and there was low voltage in all leads; the S waves were broad in Leads V_1 through V_4. A month later physical examination was negative. X-ray films of the chest demonstrated some prominence of the heart in the region of the left ventricle; bilateral apical pleural thickening was noted. An electrocardiogram showed no significant changes except for diminished T waves in Lead aVF. Three months before entry an electrocardiogram showed a normal sinus rhythm at a rate of 75; the PR and QRS intervals were 0.17 and 0.09 second, respectively; compared with the previous tracing the T waves were less diminished, and the P waves were more peaked. There continued to be episodes of palpitation that were sometimes associated with pain in both arms. During one of these episodes an observer noted tachycardia (a rate of about 120), with premature ventricular beats. Because of these episodes quinidine therapy was started a month before admission. On the morning of the day of admission he felt weak and nauseated and vomited several times. There were associated palpitation and a sensation of pressure in the chest.

At the age of two years the patient had had varicella with a high fever and three convulsions. He had sustained head trauma at the age of eleven years. There was a scalp wound but no loss of consciousness. There was no history of rheumatic fever.

Physical examination showed a thin man in moderate distress complaining of pressure in the chest and nausea. Examination of the chest was negative except for a cardiac rate of 240. Abdominal and neurologic examinations were negative.

The temperature was 98°F., the pulse 240, and the respirations 20. The blood pressure was 80 systolic, 60 diastolic.

The urine was normal. Examination of the blood revealed a hemoglobin of 14.5 gm. per 100 ml. and a white-cell count of 11,200, with 70 per cent neutrophils. The sedimentation rate was normal. The nonprotein nitrogen was 23 mg., the calcium 8.8 mg., the phosphorus 3.2 mg., the cholesterol 197 mg., the iron 190 microgm., and the fasting blood glucose 88 mg. per 100 ml. The sodium, potassium and chloride were normal. The alkaline phosphatase was 2.4 units. The serum cholinesterase activity was 0.90 delta pH per hour. A blood Hinton test was negative. A Congo-red test showed 71 per cent retention in the serum. X-ray films of the chest showed slightly more enlargement of the left ventricle than had previously been noted; there were unusually large vascular channels extending from the lung roots and a particularly wide vascular shadow behind the heart border; fluoroscopically, there was no abnormality in the pulmonary dynamics, and the heart was pulsating regularly at a rate of 100. An electrocardiogram (after procaine amide) showed a normal sinus rhythm at a rate of 75; the PR and QRS intervals were 0.18 and 0.11 second, respectively; there were broad S waves in Leads V_1 through V_3; RR′ waves were present in Leads V_4 through V_6; the T waves were low, and the P waves were enlarged in all leads.

With procaine amide given intravenously the cardiac rate returned to normal, and the blood pressure rose to 130 systolic, 80 diastolic. The heavy precordial sensation subsided, and the nausea and vomiting ceased. No cardiac murmurs were audible. There continued to be frequent episodes of spontaneous palpitation, with ventricular tachycardia associated with weakness and dizziness. During one attack there was also a sensation of numbness over the occipital region. There were no convulsions, nor was there syncope. Dilantin was discontinued, and Mebarol, 20 mg. daily, was substituted, but this had no appreciable effect in reducing the number of attacks. With increasing doses of procaine amide there was a great reduction in number and severity of attacks. X-ray films of the chest on the thirteenth hospital day showed the heart to be within the normal range in size and configuration; the pulmonary vessels were less prominent than they had previously been. An electrocardiogram showed a normal sinus rhythm at a rate of 60 to 65; the PR and QRS intervals measured 0.19 and 0.09

second, respectively; the P waves showed increased amplitude in all leads; the voltage of the QRS complexes was low in the limb leads and slightly low in the precordial leads, with a tendency to splintering without definitely abnormal axis deviation; compared with previous tracings there was a slight change in the T-wave pattern, with an improvement in amplitude in Lead 2; the T waves in Leads 3 and aVF were low and upright; the ST segments were less diphasic over the precordium than previously. The patient remained afebrile and was discharged improved on the fifteenth hospital day.

With continuation of procaine amide therapy there were no further episodes of tachycardia despite moderate activity. Physical examination a week after discharge was negative. The blood pressure was 95 systolic, 70 diastolic, in the sitting and 102 systolic, 70 diastolic, in the standing position. The hemoglobin and white-cell count were normal. An electrocardiogram and fluoroscopic examination of the chest showed no significant change. Subsequently, he lived a normal life, indulging in the usual sports. He was found dead in bed three weeks later. He had been in his usual state of health the evening before death.

Differential Diagnosis

Dr. James H. Currens*: In summary this young man was in good health until the onset of grand-mal seizures two and a half years before his death and eventually died during his sleep, presumably during an attack of ventricular arrhythmia, which was demonstrated by an electrocardiogram during a previous seizure. He had convulsions at an early age when he had high fever, which perhaps predisposed him to seizures during unusual circumstances. However, the electroencephalogram was not abnormal so that it is only a supposition that he was more subject to seizures than the average person.

Stertorous breathing was noted. Was Cheyne–Stokes breathing noted at any time? The breathing phase of Cheyne–Stokes respiration is sometimes interpreted as rapid breathing or stertorous breathing.

Dr. Gordon S. Myers: There was no Cheyne–Stokes respiration.

Dr. Currens: After unconsciousness in patients who have Adams–Stokes syndrome, Cheyne–Stokes breathing does occur. The palpitation and dyspnea that this patient had was understandable on the basis of the findings by direct observation while he was in the hospital. The pain and the aching sensation in the chest and neck extending into the arms is also understandable on the basis of a rapid ventricular rate with poor blood supply to the myocardium and is manifest as angina pectoris. The ventricular tachycardia that was demonstrated at least on one or two occasions was apparently characteristic. There was one episode, however, during which the pulse was 120 and apparently slightly irregular; one wonders whether the patient might have had, to account for some of the arrhythmia, an atrial flutter with either a 1:1 response and a ventricular rate of 240 or a 2:1 response and a rate of 120. The slight arrhythmia noted at that time would be unusual in a patient with atrial flutter. The electrocardiogram indicated normal sinus rhythm between attacks. It is important to remember that the electrocardiogram can be normal between attacks of cardiac arrhythmia even in patients who have the Adams–Stokes syndrome, so that, to make the diagnosis, one has to observe the patient or take an electrocardiogram at the time of the attack. Cardiac enlargement, mentioned in the x-ray examination, is fairly common in association with any tachycardia of several hours' duration. The fact that the cardiac enlargement was transient suggests that it was the result of a cardiac arrhythmia rather than of a structural disease of the heart itself. May we look at the x-ray films, Dr. Hanelin?

Dr. Joseph Hanelin: The initial film of the chest was made when the patient was seen in the Out Patient Department. The lungs are clear; the heart is almost normal in size; there may be slight enlargement of the left ventricle. At the time of admission the heart was distinctly larger than it was when this man was an outpatient, but in the hospital it reverted to a more nearly normal size, although it was still slightly full along the left ventricular contour. I am not impressed with any undue prominence of the pneumonic vascular shadows. The density mentioned alongside the heart may have been the inferior portion of the left interlobar artery.

Dr. Currens: Do you think that the atria are enlarged from the x-ray examination?

Dr. Hanelin: I cannot be sure of any atrial enlargement.

Dr. Currens: The seizures, or syncope, of course, were the important feature of the hospital course. It is difficult to explain these attacks on the basis of heart disease although one cannot strictly speak of this as the Adams–Stokes syndrome, because Adams[1] originally and Stokes[2] nineteen years later described patients with cerebral symptoms associated with a slow pulse; however, it has been demonstrated that the same phenomena may occur in association with tachycardia of a high degree[3] or with transient ventricular fibrillation. I should choose to explain the cerebral symptoms on this basis therefore.

It is of interest that Mr. Robert Adams,[1] and I emphasize the Mister since he was a surgeon and a distinguished member of the Royal College of Surgeons of Ireland, described the first case in 1827. He wrote, "What most attracted my attention was the irregularity of the breathing and remarkable slowness of the pulse." The irregularity of the breathing was undoubtedly Cheyne–Stokes in type because in the previous paragraph he commented on the original case that Cheyne[4] reported, which is now considered

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the classic description of Cheyne–Stokes breathing. It is interesting, therefore, that the first patient described with Adams–Stokes syndrome had Cheyne–Stokes breathing. This has been observed in other cases. In this hospital during the past year 2 patients have been observed to have Cheyne–Stokes breathing for several hours after episodes of syncope or seizure resulting from the Adams–Stokes syndrome.

In a patient with heart disease and seizures, one also has to consider the possibility of embolization to the brain from the heart, particularly when there is dilatation of the heart and possibly a mural thrombus. Pertinent to this point is the study by Richardson and Dodge,[5] from our neuropathology laboratory, of 104 case of patients with strokes, 12 per cent of whom had seizures in association with the onset of the stroke. Six of these 104, or about 6 per cent, had persistent recurrent seizures associated with cerebral infarction; 5 of the 6 cases were thought to have resulted from emboli to the brain.

The etiology of the ventricular tachycardia should be considered because that presumably caused the patient's death. In the majority of patients with ventricular tachycardia, coronary-artery disease is the underlying anatomical finding and accounts for perhaps 75 per cent of the cases. However, those patients are usually older than this patient and usually have enlargement of the heart; therefore, I think that it is unlikely that coronary-artery disease was the cause of the ventricular tachycardia. Digitalis intoxication is another cause of ventricular tachycardia, usually in patients with rheumatic heart disease. It is difficult to know what percentage to allocate to digitalis intoxication although perhaps 15 per cent would be a reasonable figure. Another type of heart disease that might account for the tachycardia is congenital heart disease, but there was nothing to indicate that the patient had any of the signs or symptoms usually seen with congenital heart disease; there was no murmur and no cyanosis. The only congenital lesion that he may have had is an interatrial septal defect because of the prominence of P waves in the electrocardiogram and suggestion of prominence of the vascular shadows on x-ray examination. I think that it is unlikely that he had an interatrial septal defect.

This patient was a chemist so I suppose that a toxic myocarditis was considered. I am not told to what chemical or group of chemicals he may have been exposed. I think it is unlikely that there was a toxic myocarditis from an industrial contact. Hemosiderosis was considered because the blood iron determination was done. Hemosiderosis sometimes affects the heart, but the heart is enlarged in such cases. I should not consider that seriously. Amyloidosis, too, was considered because a Congo-red test was done. Primary amyloidosis, which usually involves the heart, does not affect the Congo-red test so that would not be of help.

Perhaps 10 to 15 per cent of the patients with ventricular tachycardia have normal hearts as far as can be determined. Sometimes, these patients succumb during an attack, and at autopsy the heart is structurally normal. I think that is the most likely finding in this patient. There is such a case of a middle-aged woman recorded in the literature,[6] and I believe Dr. Sprague had such a case a year or so ago. Sudden death or death caused by arrhythmia of the heart occurs in other conditions, like the Wolff–Parkinson–White syndrome, so that any arrhythmia of the heart may result in sudden death, presumably as the result of ventricular fibrillation or ventricular arrest.

About the medications — Dilantin did not seem to have any effect upon the incidence of the seizures, and one would not expect it to affect them if the patient had true Adams–Stokes attacks, unless probably to make them worse. I have seen a patient with Adams–Stokes syndrome in whom Dilantin greatly increased the frequency of the attacks. Procaine amide seemed helpful in reducing the attacks, according to the protocol. Quinidine was tried for a short time in the patient under discussion, but in the patient with Stokes–Adams syndrome about whom I spoke quinidine seemed to aggravate the situation and was thought to precipitate ventricular fibrillation on one occasion. Therefore, there is some question whether quinidine is the ideal drug to use.

DR. WILLIAM H. BAKER: Does endocardial fibrosis ever produce this type of arrhythmia?

DR. CURRENS: Not in my experience. Dr. Sprague, have you experienced this?

DR. HOWARD B. SPRAGUE: I should expect cardiac enlargement under those circumstances. I think that the patient could have had a localized microscopic myocardial process. It may be true that grossly the heart appeared normal, but the pathologist may have found something microscopically. In my patient to whom Dr. Currens referred, the attacks started with ventricular premature beats and went on to ventricular tachycardia and standstill, with unconsciousness and repeated convulsions. As I understand it the gross and microscopical findings at autopsy showed nothing obviously wrong.

DR. MYERS: The patient presented quite a problem. There is a correction on the protocol; the patient did not resume the usual sports. We advised him to take a leave of absence and to stay quietly at home. He felt compelled to make a trip to Ohio to speak to his fiancée because we advised him to postpone his marriage indefinitely. He apparently had idiopathic epilepsy, apart from the cardiac irritability. The fact that he had convulsions earlier and had seizures that were not associated with bouts of arrhythmia in the past supported that idea. We were unable to make a diagnosis of any kind of heart disease, including the rare forms that Dr. Currens mentioned. Since in most series 10 to 20 per cent of the patients have normal

hearts, particularly the younger persons, and since such patients have a relatively good prognosis even if they have multiple attacks, we hoped that this patient would fall in that group, but we had to give him a guarded prognosis because we were unsure of the diagnosis.

DR. DANIEL S. ELLIS: Does Dilantin have any known effect on the electrocardiogram?

DR. MYERS: In large amounts it can be a depressive for cardiac irritability. I do not know whether it causes any widening of QRS complexes. At any rate we stopped the Dilantin because we were grasping at straws. The cholinesterase activity was measured because this patient was working with anticholinesterases in the laboratory.

DR. REED HARWOOD: What is your explanation of the prolonged QRS interval?

DR. MYERS: I had two thoughts: aberrancy of conduction during very rapid tachycardia is not unheard of by any means — it is fairly frequent even with a paroxysm of atrial tachycardia to see widening and aberrancy of the conduction in the ventricle. Secondly, this patient throughout the hospital course and thereafter when he was under my observation, was receiving large doses of procaine amide, which in itself can cause some widening of the QRS complexes. We suspected that the widening followed by improvement in the electrocardiogram and the enlargement of the heart followed by what seemed to be a return to the normal limits were the result of the facts that he had prolonged bouts of tachycardia at very rapid rates and that at such times the dosage of procaine amide given to him had also been increased.

CLINICAL DIAGNOSIS

Paroxysmal ventricular tachycardia.
?Idiopathic epilepsy.

DR. JAMES H. CURRENS'S DIAGNOSES

Paroxysmal ventricular tachycardia.
Adams–Stokes syndrome.

ANATOMICAL DIAGNOSIS

Fibrosis of myocardium, diffuse, probably secondary to myocarditis.

PATHOLOGICAL DISCUSSION

DR. WINFIELD S. MORGAN: Although this patient was studied in this hospital, he died in Ohio. We are grateful to Dr. R. C. Thomas, of the Elyria Memorial Hospital, Elyria, Ohio, for the protocol and portions of the heart for study. At autopsy this man was described as being rather asthenic but fairly well nourished. The only abnormal finding either grossly or microscopically was in the heart, which weighed approximately 225 gm. The pericardial surfaces were smooth and glistening. The heart was markedly dilated. Sections through the myocardium disclosed a marked fibrosis that was irregular in distribution and produced a nodularity that was prominent on palpation of the external surface. This fibrosis involved all portions of the musculature. The heart walls were much thinner than usual. The endocardium showed areas of thickening and opacity. This was seen on the

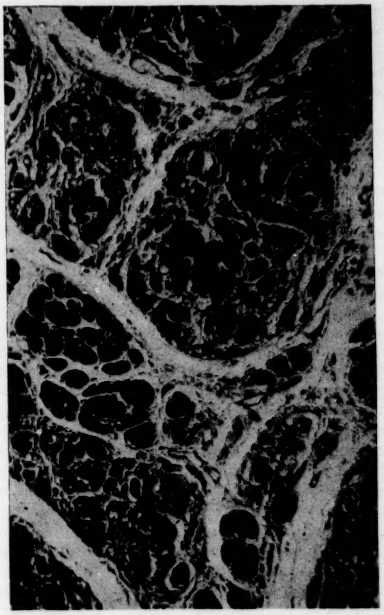

FIGURE 1.

surfaces of the columnae carneae and papillary muscles. These areas averaged 1 cm. in diameter, and the majority of the endocardial surface was smooth, glistening, thin and transparent. The heart valves were normal. Coronary ostia were patent. The coronary arteries did not have their customary anatomical distribution, however, being subdivided into many small arteries that coursed in unusual patterns across the heart surface. These vessels, however, were thin-walled, elastic and showed no disease or occlusions.

The aorta and larger arteries and veins were normal. Microscopically, our sections confirmed the gross impression that there was fibrosis of the myocardium of a diffuse nature (Fig. 1). Although occasionally such areas were subendocardial in location, a majority were deep, and the picture did not in any way suggest endocardial fibroelastosis as reported from

this laboratory by Thomas and his associates.[7] In these areas there was no inflammatory infiltration, and they simply consisted of rather acellular scar tissue. In only one section was there any inflammatory infiltration. This was a single small area in which muscle fibers were absent and in which the cellular infiltrate was not severe and consisted chiefly of lymphocytes, a few mononuclear leukocytes and a few phagocytes containing hemosiderin. Nowhere did we find any active lesions and no acute necrosis of the myocardium.

DR. CURRENS: Do you think that the scarring could have been caused by prolonged attacks of tachycardia?

DR. MORGAN: I do not know how to answer that.

DR. CURRENS: Was the brain examined?

DR. MORGAN: It was examined and was normal.

DR. SPRAGUE: I do not believe that the scarring could have been caused by the attacks because patients can have severe attacks of ventricular tachycardia, resulting even in congestive heart failure, over a period of years with eventual recovery and restoration to normal. I think the cart and horse are the other way around.

DR. MORGAN: Although one would probably immediately think from the gross and microscopical appearance that this heart represented the end stages of a diffuse myocarditis, one hesitates in jumping to that conclusion in the absence of any significant inflammatory infiltration. I think it is better to consider the case as one of diffuse myocardial fibrosis. As Dr. Currens pointed out, in a man of twenty-four and in the absence of any recognizable disease of the coronary vessels, one would not want to attribute the fibrosis to coronary-artery disease. If we exclude this possibility a previous myocarditis of some sort seems the most likely explanation. Myocarditis is classified as fetal type, which occurs in the very young; the type seen in association with an infectious disease such as diphtheria or poliomyelitis; the specific myocarditides such as are seen in rheumatic fever, tuberculosis and syphilis; and the isolated Fiedler, or idiopathic, type of myocarditis. I think we can rule out the fetal type. The clinical story does not tell us of diphtheria or other severe infectious disease in the past, and the sections did not show anything suggestive of tuberculosis or syphilis. In the absence of valvular lesions grossly or Aschoff bodies microscopically, one would not consider very seriously a diagnosis of rheumatic myocarditis. That leaves the isolated type, under which I think this case probably would be classified. The diffuse myocardial fibrosis is consistent with the idea that this young man had, sometime in the past, an isolated or idiopathic type of myocarditis that had resulted in the severe focal scarring. Moritz and Zamcheck[8] made an interesting study of sudden death in young soldiers on Army Institute of Pathology material. From about 40,000 autopsies they found some 300 young persons who died suddenly. Most of these deaths were the result of coronary occlusion, but there were about 34 with other cardiovascular lesions, of which 14 were acute and subacute myocarditis of the isolated type. In addition there were 5 cases of diffuse idiopathic myocardial fibrosis. The authors do not go into detail about these cases, but I wonder if they were not similar to our case today.

DR. ROBERT S. SCHWAB: I agreed with Dr. Myers that this patient probably had epilepsy because of the early history, the type of the seizures and the electroencephalogram, which on two occasions was mildly abnormal. I do not see any report in the record of the one normal electroencephalogram that was mentioned in the protocol.

DR. CURRENS: May I point out that the common cause of "myocarditis" of old or what is now referred to as myocardial scarring is ischemia of the muscle? This patient did have angina pectoris associated with some of his attacks of tachycardia, but there was no evidence of coronary-artery disease.

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Dr. Scott Alison has exhibited an instrument to the Royal Society which he calls a sphygmoscope, and employs to indicate the movements of the heart and bloodvessels.

Boston M. & S. J. *May 8, 1856*

The New England Journal of Medicine

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY

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THE ANNUAL MEETING

AN editorial note has already been published regarding the significance of the current anniversary of the founding of the Massachusetts Medical Society, and elsewhere in this issue of the *Journal* the program of the oncoming annual meeting of the Society is to be found. The Society has been in continuous existence for seventeen and a half decades; a record of the exact number of annual meetings that have been held is not immediately available but is short of a hundred per cent. In the early days meetings were occasionally omitted, as occurred perforce during the war.

The meeting, which will be held in Boston at the Hotel Statler, will follow the same general pattern that has prevailed for several years. The Council will meet in the late afternoon and evening of Monday, May 21, a meeting pleasantly interrupted by the traditional Cotting Supper. The general sessions will start on the following morning and will continue through Thursday, May 24, with appropriate interludes.

The first of these will be the official annual meeting of the Society on Tuesday afternoon, at which awards will be presented to a carefully selected student from each of the three medical schools of the Commonwealth, and one to a layman for outstanding contributions to medical progress. Badges will be presented to a group of fellows of the Society who have, since the last meeting, surmounted their fiftieth year in practice, and a certificate will be presented to the retiring president, who, on the same occasion, will deliver his "state of the union message." The *pièce de résistance* will be supplied by Dr. Merrill C. Sosman, professor of radiology at Harvard Medical School and radiologist-in-chief of the Peter Bent Brigham Hospital, in the form of the annual oration or discourse on the subject *Docendo Discimus*, which, Dr. Sosman suggests, has no intervertebral significance.

At precisely 11:05 on the morning of Wednesday, May 23, Dr. Chester M. Jones, clinical professor of medicine, Harvard University, and visiting consultant in medicine at the Massachusetts General Hospital, will deliver the annual Shattuck Lecture of the Society on "Changing Concepts and Practices in the Approach to Diseases of the Digestive Tract." On the evening of the same day the annual dinner will take place, with the Honorable Leverett A. Saltonstall, senior senator from Massachusetts, as guest speaker.

As ancillary events the annual golf tournament will be held at the Dedham Country and Polo Club on May 23, the American Medical Women's Association, Branch 39, will hold a luncheon meeting, and the Massachusetts Medico-Legal Society will meet in the afternoon. The usual exhibition of works of art by members of the Massachusetts Physicians Art Society will be held elsewhere in the hotel.

The Woman's Auxiliary to the Society will meanwhile be conducting its own festivities at the Hotel Somerset. The annual business meeting, under the presidency of Mrs. John Angley, will take place at 10:00 a.m. on Tuesday, May 22, and will be followed by a luncheon at which the guest speaker will be the national president, Mrs. Mason G. Lawson, of Little Rock, Arkansas. In the afternoon a reception will be held at the Statler in honor of Mrs. Lawson and the past presidents of the State Auxiliary.

The tour on the following day will take the members to the Blacksmith Shop Restaurant in Whitman for luncheon and a dramatic entertainment.

The fellows of the Society are reminded that at the scientific and technical exhibits more things will be displayed than can be found in Heaven, Hell or Hoboken, as the poet expressed it.

GOVERNMENT AND MEDICAL RESEARCH

OVER a year ago former Secretary Hobby, of the Department of Health, Education and Welfare, requested the National Science Foundation to appraise the medical-research programs and problems of the various agencies of the Department so engaged. To this end a special committee of scientists under the chairmanship of Dr. C. N. H. Long, of Yale University School of Medicine, was organized, which began work in July, 1955, and submitted its report in December. The report was released in March of this year.

The business of big-time government-supported medical research is one of the big, new activities in a world full of big, new activities, having started on its present burgeoning course during the war. It was then an urgent adjunct to the relatively placid academic research of ante-bellum days, carried out in universities and medical schools and supported by private philanthropy. All now is changed, with every eye turned to Washington and with a Congress almost stubbornly eager to finance point by point the solution of the many and intricate problems of health. Under such a mandate not only has the Public Health Service undergone an unprecedented scientific expansion but various other agencies have come into existence or burst into renewed activity. Most of them are administered by the Department of Health, Education and Welfare, and any Secretary would naturally want to know the ins and outs to the road that she or he is expected to follow.

The programs of research in medicine and health have been centered largely in four agencies of the Department: the Social Security Administration, containing the Children's Bureau; the Office of Vocational Rehabilitation; the Food and Drug Administration and the Public Health Service, including the Bureau of State Services (services to the states) and the National Institutes of Health with their intramural and extramural programs. All these agencies have been fulfilling their investigative obligations within the limitations imposed on them by the terms of their original establishment. The Children's Bureau and the Office of Vocational Rehabilitation, the Committee found, have been co-ordinating well with other agencies and should be able to carry on their research activities at a cost of a millon dollars a year apiece. The Food and Drug Administration, suffering perhaps from a mild case of segregation, needs to establish better communication with its fellow agencies in the Department, except for the National Institutes of Health, where relations are reasonably intimate; legislation is needed to make manufacturers supply data on essential toxicity with respect to food and cosmetic additives, as has long been done in the case of drugs.

The Bureau of State Services of the Public Health Service is pursuing its original objective of aiding the separate states in matters of personal health and the environmental factors that bear on health. Its research program has been conducted at a cost of $7,500,000 a year, although an increase of $4,200,000 has been requested.

The National Institutes of Health, the youngest and the largest of the federal agencies engaged in medical research, has come into being for the explicit purpose of conducting and supporting "research into the cause, diagnosis, prevention, and treatment of the diseases and disabilities of man." The institutes, 7 in number like the branches of a candelabrum, are established on a categorical basis, each being oriented toward a specific disease group.

Financed by an annual budget for research that has increased from $53,500,000 in 1953 to $97,500,000 in 1956 their activities are divided into the intramural program of research conducted at each institute and the Clinical Center at Bethesda, and the extramural program, consisting of investigations conducted here and there on grants from the central sources. These disbursements amount to two thirds of the research budget and are allocated, under a watchful if not always discriminating congressional eye, also on a categorical basis.

It is in this relation that the Committee makes its most emphatic recommendations, in respect to the categorical distribution of allotments regardless of the freedom of thought and action required for the best performance at the highest levels. Such a method of specific allocations leads to the belief on the part of the public that a desired result is purchasable; that effective research in any line can be bought like yard goods and made into a finished product by skilled craftsmen drawn from an inexhaustible labor pool. The emphasis is taken away from the necessity of finding the right individuals, freeing them from Civil Service requirements, paying them according to their qualifications and giving them economic security and intellectual freedom. Democratic governments, in this respect, seem dedicated to a policy of extravagant

niggardliness, erecting sumptuous facilities at the expense of high-quality personnel. Consequently, the Committee has recommended a board of scientists to approve matters of general policy, appointments and promotions within the institutes.

So far as the extramural programs of the National Institutes of Health are concerned, the Committee finds that faith has generally been kept in regard to noninterference with the administration of the functions of the institutions to which grants are made. Also, as far as possible, money that has been promised for successive years in extended projects has been forthcoming. Here, again, the greatest weakness is the categorical allocation of grants as required by present law, not only restricting the effectiveness of research but sometimes actually adding to the financial embarrassment of the schools that have been thus favored, not utterly unlike the distribution of cuckoos' eggs in nests where no provision has been made for their accommodation.

Here the Committee concludes that a final new agency is needed in the Department — an "Office of Medical Research and Training" to administer the support of extramural research activities and the training of scientists to undertake them. It is devoutly to be hoped that Congress, in whose hands the appropriations rest, will have the vision to see this opportunity for service in its entirety, and the wisdom to accept genuinely disinterested advice.

NATIONAL ACADEMY OF RELIGION AND MENTAL HEALTH

THE psychiatrists, theologians, sociologists and others who have participated in preliminary discussions for the past three years and whose efforts have culminated in the organization of the National Academy of Religion and Mental Health deserve every acclaim for what they have done and for what they are setting out to do. No doubt, as their efforts become more and more integrated, their horizons will become even broader, and the scope of their accomplishments much more far reaching than is now apparent, possibly even to them. This organization is unique not only in this country but in the world. The idea of it has been about for a long time, but the putting of these ideas and words into action is indeed most praiseworthy. One of the objectives, preventive mental health, has many ramifications. Not only the psychotic, neurotic, or hypochondriac person, the alcoholic or narcotic addict and the juvenile delinquent but also the normal man, woman and child will benefit from this program.

The thought that science and religion agree has permeated contemporary society. Just as there are scientific laws, so too there are spiritual laws, each of which is revealed to man according to man's capacity to find it; where inconsistencies between science and religion appear they are man-made misinterpretations of religion or man-made miscalculations in the field of science. Man has taught his fellow man many errors under the guise of religion, disregarding or misinterpreting the divine manifestations that have been revealed to him. Similarly, in the field of science, man once taught that the world was flat, and the majority believed it. This did not make it true. Truth is truth and is not measured by the numbers believing.

In this ever-evolving, maturing civilization man is slowly realizing that he has the right to investigate truth independently. When the first settlers came to this country they wished to have the legal right to worship as they pleased. Today, man has this legal right, but too frequently he has lost true religious liberty. Many have lost freedom from self, freedom from prejudice and freedom from tradition. The great pacifist, Tolstoy, wrote, "The man who holds the key to the universe is a Persian named Bahá-u-lláh." Bahá-u-lláh taught the importance of independent investigation of truth and revealed that pure science and pure religion do not disagree. Perhaps the Baha'i writings have many of the answers that the theologians and the psychiatrists and mankind as a whole are seeking.

For many years the noted historian, Arnold Toynbee, has advocated that the possible solution to the world's problems is a renewal of religion and a bringing together of the religions of the world.

The newly formed National Academy of Religion and Mental Health is making a pioneer endeavor to promote research and education in all relations between religion and health, particularly mental health. To do this the Academy has been organized on an interfaith and multidisciplinary basis.

The board of trustees and the advisory council of the Academy present a most imposing array of names. Authorities in psychiatry, theology, sociology, cultural anthropology and psychology are all there, and the *esprit de corps* with which such an organization has been established for consultative and advisory services and for research in investigation of truth is tremendous.

PROMETHEUS BOUND

BOUND sturdily in boards the twelve issues of the *Tufts Medical Alumni Bulletin* — a significant number — comprising volumes 11 through 14 for the years 1952-1955 would stand appropriately on any alumnus's five-foot shelf.

The value of the alumni bulletin as a means of practical and spiritual communication with their graduates is now recognized by schools and colleges the country over, and the bulletin of the alumni association of Tufts University School of Medicine, under its able editorship, has risen regularly to the occasion. Like Prometheus before the binding, it has proved that fire is where you kindle it.

OFFICERS OF THE MASSACHUSETTS MEDICAL SOCIETY, 1955–1956

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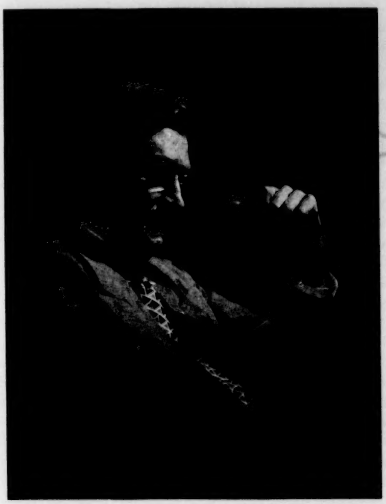

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ONE HUNDRED AND SEVENTY-FIFTH ANNIVERSARY OF THE MASSACHUSETTS MEDICAL SOCIETY

Tuesday, Wednesday and Thursday, May 22, 23 and 24

Hotel Statler, Boston

Committee on Nominations

The Committee on Nominations has presented the following slate to be voted upon by the Council at its annual meeting, May 21, 1956.

President: Dr. Howard F. Root, Brookline
President-elect: Dr. Patrick J. Sullivan, Dalton
Vice-President: Dr. Leopold F. King, Lowell
Secretary: Dr. Robert W. Buck, Waban
Treasurer: Dr. Eliot Hubbard, Jr., Cambridge
Assistant Treasurer: Dr. Norman A. Welch, West Roxbury
Orator: Dr. Paul D. White, Belmont

Delegates to the American Medical Association:
January 1, 1957 — December 31, 1958
Dr. Charles G. Hayden, West Newton; Dr. John F. Conlin, Winchester, *alternate*
Dr. Lawrence R. Dame, Greenfield; Dr. H. Thomas Ballantine, Jr., Dedham, *alternate*
Dr. Philip S. Foisie, Milton; Dr. Lewis S. Pilcher, West Newton, *alternate*

May 22, 1956 — December 31, 1957
Dr. Henry F. Howe, Cohasset, to fill the unexpired term of the late Dr. Harold R. Kurth; Dr. Donald R. Hayes, Longmeadow, *alternate*

Robert W. Buck, M.D., *Secretary*

Program

The Registration Desk will be located on the mezzanine floor, and all who attend the meeting are requested to register. The following events take place on the day prior to the official opening of the meeting.

MONDAY AFTERNOON, MAY 21

3:30 **Supervising Censors' Meeting** (Parlor B).

5:00 **Annual Meeting of the Council** (Georgian Room).

MONDAY EVENING, MAY 21

7:00 **Cotting Supper for Councilors** (Parlors A and B).

TUESDAY MORNING, MAY 22

First General Session

Georgian Room

9:00 *The Advent of Ether Anesthesia.* An historical film in commemoration of one important event in the 175-year history of the Massachusetts Medical Society.

9:25 to 10:15 **Panel Discussion:** *Current Status of the Treatment of Hypertension.* Dr. Edward D. Freis, Moderator, adjunct clinical professor of medicine, Georgetown University School of Medicine; chief, Medical Service, Veterans Administration Hospital, Washington, D. C.
Dr. William Hollander, instructor in medicine, Boston University School of Medicine; associate member, Evans Memorial Hospital.
Dr. James H. Currens, assistant in medicine, Massachusetts General Hospital; associate physician, Boston Lying-in Hospital.

10:40 **Recess.**

11:05 *Ultrasound As an Adjunct to Physical Therapy.* Dr. Justus F. Lehmann, associate director, Department of Physical Medicine, The Ohio State University, Columbus, Ohio.

11:30 *Some Preoperative Warnings of Operating Room Deaths.* Dr. James E. Eckenhoff, professor of anesthesiology, School of Medicine and Graduate School of Medicine, University of Pennsylvania Hospital.

TUESDAY NOON, MAY 22

Section Meetings and Luncheons

12:00 m. — 2:00 p.m.

Section of Medicine

Parlor A

Dr. Ralph H. Wells, Lexington, *Chairman*
Dr. Harold F. Brown, Newton Centre, *Vice-Chairman*
Dr. Francis G. Barnum, Jr., Brookline, *Secretary*

A Technique for Administering the Antihypertensive Drugs. Dr. Edward D. Freis, adjunct clinical professor of medicine, Georgetown University School of Medicine; chief, Medical Service, Veterans Administration Hospital, Washington, D. C.

Section of Radiology

Parlor B

Dr. Martin H. Wittenborg, Boston, *Chairman*
Dr. Joseph F. Zielinski, Holyoke, *Secretary*

Education in Radiology. Dr. Shields Warren, professor of pathology, Harvard Medical School; director, Cancer Research Institute, New England Deaconess Hospital; pathologist, New England Deaconess Hospital.

Section of Physical Medicine

Parlor C

Dr. William J. Shriber, Boston, *Chairman*
Dr. Bernard J. Doyle, Boston, *Secretary*

Biophysic and Physiologic Research as a Basis for Ultrasonic Therapy. Dr. Justus F. Lehmann, associate director, Department of Physical Medicine, The Ohio State University, Columbus, Ohio.

Section of Anesthesiology

Parlors D and E

Dr. Philip S. Marcus, Boston, *Chairman*
Dr. William J. Martin, Jr., Worcester, *Secretary*

Some Hazards in the Use of Succinylcholine. Dr. James E. Eckenhoff, professor of anesthesiology, School of Medicine and Graduate School of Medicine, University of Pennsylvania Hospital.

TUESDAY AFTERNOON, MAY 22

2:30 **Annual Meeting of the Massachusetts Medical Society** (GEORGIAN ROOM).

Presentation of Awards to Medical Students

An Award for Outstanding Contributions by a Layman to Medical Progress

Presentation of Badges to Fifty-Year Members

Presentation of Certificate to the Past President

Annual Discourse: *Docendo Discimus.* DR. MERRILL C. SOSMAN, professor of radiology, Harvard Medical School; radiologist-in-chief, Peter Bent Brigham Hospital.

WEDNESDAY MORNING, MAY 23

Second General Session

GEORGIAN ROOM

9:00 *General Practice and Mental Retardation.* DR. THOMAS A. KELLEY, obstetrician, Somerville Hospital.

9:05 *Tuesday's Child.* (A motion picture.)

9:25 *The Organic Basis of Mental Deficiency.* DR. DOUGLAS BUCKMAN, professor of neurology, University of Chicago.

9:50 *The Sears Foundation Medical Aid Program.* DR. LAWRENCE R. DAME, New England Representative, Medical Advisory Board.

10:15 *Pathological Changes in Maternal Deaths.* DR. DONALD G. MCKAY, pathologist, Boston Lying-in Hospital and Free Hospital for Women.

10:40 **Recess.**

11:05 THE SHATTUCK LECTURE. *Changing Concepts and Practices in the Approach to Diseases of the Digestive Tract.* DR. CHESTER M. JONES, clinical professor of medicine, Harvard University; visiting consultant in medicine, Massachusetts General Hospital.

WEDNESDAY NOON, MAY 23

Section Meetings and Luncheons

12:00 m. — 2:00 p.m.

Section of Obstetrics and Gynecology

PARLOR B

DR. SMITH G. PHILIPS, Worcester, *Chairman*
DR. ARCHIE A. ABRAMS, Boston, *Vice-Chairman*
DR. JAMES S. KAVANAH, Brookline, *Secretary*

Changing Maternal Mortality in Massachusetts. DR. JOHN FIGGIS JEWETT, chairman, Committee on Maternal Welfare, Massachusetts Medical Society; assistant in obstetrics, Harvard Medical School; assistant obstetrician, Boston Lying-in Hospital; assistant surgeon, Free Hospital for Women.

Section of Pediatrics

PARLOR C

DR. MAURICE T. BRIGGS, Lynn, *Chairman*
DR. MARSHALL B. KREIDBERG, Boston, *Secretary*

Some Surgical Problems of Infancy and Childhood. DR. ORVAR SWENSON, clinical professor of pediatric surgery, Tufts University School of Medicine; surgeon-in-chief, The Boston Floating Hospital for Infants and Children.

Section of Physiology and Pathology

PARLORS D AND E

DR. JOHN D. HOUGHTON, Milton, *Chairman*
DR. JAMES H. GRAHAM, Melrose, *Vice-Chairman*

The Pathogenesis of Atherosclerosis. DR. GEORGE V. MANN, surgeon (R), U. S. Public Health Service, Heart Disease Epidemiology Study of the National Heart Institute.

Section of Industrial Health

PARLOR A

DR. THOMAS P. KENDRICK, Boston, *Chairman*
DR. ROBERT B. O'CONNOR, Boston, *Secretary*

The ABC's of Noise in Industry. MR. CHARLES R. WILLIAMS, associate professor of applied industrial hygiene, Harvard School of Public Health; director of Industrial Hygiene Services, Liberty Mutual Insurance Company.

WEDNESDAY AFTERNOON, MAY 23

Third General Session

GEORGIAN ROOM

SURGICAL CARE — The Massachusetts Medical Society in co-sponsorship with the American College of Surgeons Committee on Nutrition and Postoperative Management.

2:00 to 5:00 **Symposium.** DR. FRANCIS D. MOORE, Moderator, Moseley Professor of Surgery, Peter Bent Brigham Hospital, Boston.

The Management of Patients Undergoing Surgery for Portal Hypertension. DR. CHARLES G. CHILD, III, professor of surgery, Tufts University School of Medicine; director, First (Tufts) Surgical Service, Boston City Hospital.

The Excretion of Water and Solutes in Relation to Diuresis and Antidiuresis. DR. JOHN D. CRAWFORD, assistant professor of pediatrics, Harvard Medical School.

Management of Patients Undergoing Surgery for Mitral and Aortic Stenosis. DR. HARRISON BLACK, instructor in surgery, Harvard Medical School; associate in surgery, Peter Bent Brigham Hospital.

Problems of Digitalization in the Cardiac Surgical Patient. DR. BERNARD LOWN, assistant in medicine, Peter Bent Brigham Hospital.

Coagulation Defects in Surgical Patients. DR. FRANK H. GARDNER, associate in medicine, Harvard Medical School; associate in medicine, Peter Bent Brigham Hospital.

The Effects of Excessive Citrate Infusion in Children. DR. ROBERT M. SMITH, anesthesiologist, the Children's Hospital.

Antibiotic-Resistant Bacterial Infection. DR. EDWARD H. KASS, assistant professor of medicine, Harvard Medical School; assistant physician, Thorndike Memorial Laboratory, Boston City Hospital.

Some Observations on Severe Burns with Particular Reference to the Mortality Rate. DR. BENJAMIN A. BARNES, instructor in surgery, Harvard Medical School; assistant in surgery, Massachusetts General Hospital.

WEDNESDAY EVENING, MAY 23

6:00 - 7:00 **Cocktail Party** (PARLORS A, B AND C).

7:00 **Annual Dinner of the Massachusetts Medical Society** (GEORGIAN ROOM).

Presiding: DR. CONRAD WESSELHOEFT, president, Massachusetts Medical Society.

Guest Speaker: THE HONORABLE LEVERETT A. SALTONSTALL.

Ladies may be invited to attend the dinner.

Tickets for the cocktail party and dinner must be procured in advance.

THURSDAY MORNING, MAY 24

Fourth General Session

GEORGIAN ROOM

9:00 *"Cardiac Arrest."* (A motion picture.)

9:25 to 10:40 **Symposium,** *"Cardiac Arrest."* DR. ALLAN L. FRIEDLICH, JR., instructor in medicine, Harvard Medical School; assistant physician, Massachusetts General Hospital.
DR. PAUL R. HINCHEY, surgeon, Salem Hospital.
DR. MORRIS J. NICHOLSON, anesthetist, Lahey Clinic.

10:40 **Recess.**

11:05 *A Critique of the Tranquilizing Drugs in Neuropsychiatry.* DR. HARRY FREEMAN, director of research, Worcester State Hospital.

11:35 *Use of Platelet Transfusions and Blood Fractions in the Treatment of Bleeding.* DR. MARIO STEFANINI, assistant professor of medicine, Tufts University School of Medicine; director of research and hematologist, St. Elizabeth's Hospital.

THURSDAY NOON, MAY 24

Section Meetings and Luncheons

12:00 m. — 2:00 p.m.

Section of Surgery

PARLOR B

DR. FREDERICK P. ROSS, Fitchburg, *Chairman*
DR. DOUGLAS A. FARMER, Boston, *Secretary*

That Controversial Thyroid Nodule. DR. GEORGE CRILE, JR., Director, Cleveland Clinic.

Section of Dermatology

PARLOR A

DR. WILLIAM R. HILL, JR., Boston, *Chairman*
DR. PAUL J. CATINELLA, Boston, *Secretary*

Dermatologic Therapy of Yesterday and Today. DR. ALFRED HOLLANDER, assistant professor of clinical dermatology, Boston University School of Medicine; associate dermatologist, Massachusetts Memorial Hospitals; dermatologist, Wesson Memorial Hospital, Springfield.

Section of Ophthalmology and Otolaryngology

PARLOR C

DR. EDGAR M. HOLMES, Boston, *Chairman*
DR. LAWRENCE R. DAME, Greenfield, *Vice-Chairman*
DR. JOHN E. McKEIGUE, Arlington, *Secretary*

The Problem of Unilateral Exophthalmos. DR. RICHARD B. PIPPITT, staff of the Massachusetts Eye and Ear Infirmary, Massachusetts General Hospital and the Newton-Wellesley Hospital.

Section of Psychiatry and Neurology

PARLOR A

DR. BARDWELL H. FLOWER, Worcester, *Chairman*
DR. RAYMOND D. ADAMS, Boston, *Secretary*

Critical Appraisal of the Therapy of Cerebral Vascular Diseases. DR. MILLER FISHER, assistant clinical professor of neurology, Harvard Medical School; associate neurologist, Massachusetts General Hospital.

THURSDAY AFTERNOON, MAY 24

Fifth General Session

GEORGIAN ROOM

2:00 *Noise-Induced Hearing Loss.* WALTER A. ROSENBLITH, Ing. Rad. (Bordeaux, France), associate professor of Communications, Biophysics, M. I. T.

2:25 *Observations on the Recent Polio Epidemic in Massachusetts.* DR. LOUIS WEINSTEIN, associate professor of medicine, Boston University School of Medicine; chief, Department of Infectious Diseases, Massachusetts Memorial Hospitals.

2:50 *The Community Blood Program.* DR. DONALD E. BROWN, Director of Laboratories, Hackensack Hospital, Hackensack, N. J.

3:15 to 5:00 **Panel Discussion.** *Cancer and the Surgeon.* DR. EDWARD D. CHURCHILL, Moderator, John Homans Professor of Surgery, Harvard Medical School; chief, General Surgical Services, Massachusetts General Hospital.
DR. GEORGE CRILE, JR., director, Cleveland Clinic.
DR. J. ENGLEBERT DUNPHY, director, 5th Surgical Service and the Sears Surgical Laboratory, Boston City Hospital; professor of surgery, Harvard Medical School.
DR. LANGDON PARSONS, professor, gynecology, Boston University School of Medicine; chief, gynecology, Massachusetts Memorial Hospitals.
DR. GRANTLEY W. TAYLOR, assistant clinical professor of surgery, Harvard Medical School; visiting surgeon, Massachusetts General Hospital.

SCIENTIFIC EXHIBITS

BOOTH NO.

82 — BLUE CROSS–BLUE SHIELD INFORMATION.
Sponsors: Massachusetts Hospital Service and Massachusetts Medical Service.

83 — PURPOSE, POLICIES AND ACTIVITIES OF THE ADOLESCENT UNIT.
Sponsor: The Adolescent Unit, the Children's Hospital.
Exhibitors: Dr. Felix P. Heald, Dr. Robert P. Masland, Jr., and Dr. James Roswell Gallagher.

84 — 85 — 86 — Exhibited by Massachusetts Civil Defense Agency.
Sponsor: Massachusetts Civil Defense Agency.

87 — INTRAVENOUS CHOLANGIOGRAPHY.
Sponsor: The Lahey Clinic.
Exhibitors: Dr. Robert E. Wise and Dr. Kenneth W. Warren.

88 — THE SURGERY OF ABDOMINAL ANEURYSMS.
Sponsor: The Peter Bent Brigham Hospital.
Exhibitors: Dr. Richard Warren and Dr. Chilton Crane.

89 — CARCINOMA OF THE COLON AND RECTUM.
Sponsor: The Lahey Clinic.
Exhibitors: Dr. Richard B. Cattell, Dr. Neil W. Swinton and Dr. Bentley P. Colcock.

90 — REHABILITATION STUDIES.
Sponsor: The Bay State Medical Rehabilitation Clinic.
Exhibitors: Dr. Arthur L. Watkins and staff of the Bay State Rehabilitation Clinic.

91 — YOUR HEART ASSOCIATION SERVES THE PHYSICIAN.
Sponsor: The Massachusetts Heart Association, Inc.

LADIES' PARLOR—TUBERCULOSIS OF THE SKIN: (Long-Term Observations Following Therapy with Isonicotinic Acid Hydrazide).
Sponsors: Department of Dermatology, Harvard Medical School and the Massachusetts General Hospital.
Exhibitors: Dr. Robert F. Tilley, Dr. John Adams, Jr., Dr. Chester N. Frazier, Dr. Robert Griesemer and Dr. George Odland.

CORRIDOR — MENTAL RETARDATION AND SPECIAL EDUCATION.
Sponsors: Massachusetts Department of Mental Health and Department of Education.

TECHNICAL EXHIBITORS
1956

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Ames Company, Inc.	73
Ayerst Laboratories	75
Baby Development Clinic	13
Chester A. Baker Laboratories, Inc.	64
The Baker Laboratories, Inc.	24
Bilhuber-Knoll Corporation	47
Boston Medical Library	Stage C
Boston Service Exchange	4
Brewer & Company, Inc.	45
Brown and Connolly, Inc.	Stage B
Buffington's, Inc.	55
Burroughs Wellcome & Company, Inc.	27
Cambridge Instrument Company, Inc.	7
S. H. Camp and Company	5
Carnation Company	51
Ciba Pharmaceutical Products, Inc.	31 & 32
Otis Clapp & Son	6
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Coles Electronic Corporation	9
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H. G. Fischer & Co.	77
C. B. Fleet Company, Inc.	40
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Gerber Products Company	71
Lawrence E. Gott	53
Gray Pharmaceutical Co., Inc.	64-A
H. J. Heinz Company	23
Hoffmann-La Roche, Inc.	20
H. P. Hood & Sons	58
Hornblower & Weeks	15
George Laben	29
Lederle Laboratories	26
Eli Lilly and Company	33 & 34
M & R Laboratories (see Ross Laboratories)	68
E. F. Mahady	36 & 39
Maltex Company	57
S. E. Massengill Company	17
McNeil Laboratories, Inc.	54
Mead Johnson & Company	28
Medical Clearing Bureau, Inc.	7-A
The Medical Protective Company	30
The Wm. S. Merrell Company	52
The National Drug Company	37
Nepera Chemical Company, Inc.	8-A
New England Dairy and Food Council	62
New England Journal of Medicine	Stage A
Parke, Davis and Company	67
The E. L. Patch Company	22
Pet Milk Company	66
Pfizer Laboratories	79
Postgraduate Medical Institute	Stage D
Professional and Hospital Equipment Company	10
The Purdue Frederick Company	80
R. J. Reynolds Tobacco Company	65
Riker Laboratories, Inc.	18
A. H. Robins Company, Inc.	50
J. B. Roerig and Company	61
Ross Laboratories (formerly M & R Laboratories)	68
Sanborn Company	11
Sandoz Pharmaceuticals	14
Schering Corporation	74
G. D. Searle & Company	72
Sharp & Dohme	81
Smith, Kline & French Laboratories	46
E. R. Squibb & Sons	48
Tailby-Nason Company	21
U. S. Vitamin Corporation	8
The Upjohn Company	78
Varick Pharmacal Company, Inc.	59
Walker Laboratories, Inc.	92
Warner-Chilcott Laboratories	56
White Laboratories, Inc.	35
Winthrop Laboratories, Inc.	43
Wyeth	70

ANNUAL GOLF TOURNAMENT

WEDNESDAY AFTERNOON, MAY 23
Starting Time: 1:00 p.m.
DEDHAM COUNTRY AND POLO CLUB
Dedham, Massachusetts
All members and guests are welcome.

AMERICAN MEDICAL WOMEN'S ASSOCIATION
Branch 39

WEDNESDAY, MAY 23
LUNCHEON MEETING
Hancock Room, Hotel Statler
12:00 m. — 2:30 p.m.

THE MASSACHUSETTS MEDICO-LEGAL SOCIETY

ANNUAL MEETING
WEDNESDAY AFTERNOON, MAY 23
Parlor C, Hotel Statler
2:30 p.m.

EXHIBITION OF WORKS OF ART

BY
MEMBERS OF THE
MASSACHUSETTS PHYSICIANS
ART SOCIETY
Fourth Floor, Hotel Statler
Daily: 9:00 a.m. — 5:00 p.m.
MAY 22, 23 and 24

WOMAN'S AUXILIARY TO THE MASSACHUSETTS MEDICAL SOCIETY

The registration desk for the meeting on May 22 will be in the lobby, Hotel Somerset, with registration from 9 a.m. to 4 p.m., and the registration desk for the meeting on May 22 will be in the mezzanine, Hotel Statler, with registration from 9:00 a.m. to 10:30 a.m.

TUESDAY MORNING, MAY 22

10:00 a.m. **Annual Meeting** (REGENCY BALLROOM, HOTEL SOMERSET).

TUESDAY AFTERNOON, MAY 22

12:45 p.m. **Luncheon** (REGENCY BALLROOM, HOTEL SOMERSET; $3.30, including Tax and Tip).
2:15 p.m. **Afternoon Session** (HOTEL SOMERSET).
3:30 p.m. **Executive Board Meeting.**
5:00 p.m. **Open House** (AUXILIARY SUITE, HOTEL STATLER).

WEDNESDAY MORNING, MAY 23

10:30 a.m. **Bus Tour Starting from Columbus Avenue Entrance of the Hotel Statler for the Arnold Arboretum.** (Transportation provided.)

WEDNESDAY AFTERNOON, MAY 23

1:15 p.m. **Luncheon** (BLACKSMITH SHOP RESTAURANT, WHITMAN; $2.75, including Tax and Tip).

WEDNESDAY EVENING, MAY 23

6:00 p.m. **Cocktail Party** (with members of the Massachusetts Medical Society, Hotel Statler).
7:00 p.m. **Dinner** (with members of the Massachusetts Medical Society, Hotel Statler).

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Post-Partum Hemorrhage from Uterine Atony

A thirty-year-old gravida II, para I, was admitted to the hospital at term in early labor. The first stage of labor lasted two and three-quarter hours, and the second stage thirty minutes, during which the membranes ruptured spontaneously. Spontaneously, a living infant weighing 2.6 kg. (5 pounds, 15 ounces) was delivered over a median episiotomy under light ether anesthesia. The apparently intact placenta followed in ten minutes, and Pitocin and Ergotrate were given routinely.

The patient was returned to her room in good condition, and the physician left about forty-five minutes later. An hour after delivery the fundus was boggy, and vaginal bleeding profuse. Ergotrate was given intravenously, after which the fundus contracted and bleeding ceased. The blood pressure was 80 systolic, 50 diastolic, and the pulse 110. The patient's condition at this time caused no alarm, but she is said to have been observed at ten-minute intervals.

However, half an hour later, bleeding recurred; the blood pressure was recorded as 68 systolic, 0 diastolic. Her physician and a consultant were summoned while 500 ml. of saline solution was started and stimulants were given. Plasma was also started. At this time, the patient appears to have been failing rapidly, for the hospital superintendent and the priest were also notified, and blood transfusion was ordered.

Her physicians arrived shortly afterward to find her in extremis. Pitocin was added to the intravenous solution because the fundus was soft and boggy. The patient was transferred back to the delivery room, where additional stimulants were given, but she died two hours and twenty minutes after delivery. No transfusion had been started.

Pelvic examination just before death revealed enormous clots but no lacerations in the uterus or vagina.

This case was classified as a preventable death due to post-partum hemorrhage attendant upon uterine atony. The primary avoidable factors were listed as delay in treatment and the absence of blood transfusion. There is an ominous similarity among cases of post-partum hemorrhage, and this one is no exception. With others in mind, one cannot help wondering whether the patient's fundus was literally held by an attendant for forty-five minutes after the completion of the third stage; it is assumed that it was not, since profuse bleeding rarely occurs under these circumstances and, if it does, can be corrected rapidly. Regardless of this, however, it seems in the case at hand that a warning was noted one hour post partum when profuse vaginal bleeding occurred and the patient received Ergotrate intravenously. With a blood pressure of only 80 systolic, 50 diastolic, and a pulse of 110, undoubtedly serious blood loss had already occurred; it is assumed that the volume of blood that had been lost was grossly underestimated. This is a tragic but very frequent fact in cases of this sort. Undoubtedly, a transfusion should have been started at this time. The rest of the story was typical: the patient went into irreversible shock while plasma and saline solution were given instead of the only effective remedy — namely, banked blood in large quantities. With modern typing and crossmatching facilities, the hazards of blood transfusion have been reduced, and although there are risks, they are certainly less than those of post-partum hemorrhage.

John Figgis Jewett, M.D.
Chairman

DEATH

Lowell — Alverne P. Lowell, M.D., of Fitchburg, died on March 14. He was in his eighty-fourth year.

Dr. Lowell graduated from the University of Vermont College of Medicine in 1897. He was a former head of the surgical staff at Burbank Hospital and a member of the board of trustees. He was a fellow of the American Medical Association and the American College of Surgeons and a member of the New England Obstetrical and Gynecological Society.

He is survived by his widow, two daughters and a son.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MARCH, 1956

RÉSUMÉ

Disease	March 1956	March 1955	Seven-Year Median
Chancroid	3	2	2
Chicken pox	2647	2589	2412
Diphtheria	3	3	4
Dog bite	917	1005	891
Dysentery, bacillary	2	25	15
Encephalitis, infectious	1	5	5
German measles	596	577	577
Gonorrhea	168	189	174
Granuloma inguinale	0	1	1
Hepatitis, infectious	36	125	37
Lymphogranuloma venereum	1	1	1
Malaria	0	1	0
Measles	595	11388	1835
Meningitis, meningococcal	8	5	7
Meningitis, Pfeiffer bacillus	3	3	3
Meningitis, pneumococcal	3	1	3
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	0
Meningitis, undetermined	12	8	5
Mumps	391	1797	1758
Poliomyelitis	0	1	1
Salmonellosis	36	22	11
Scarlet fever	868	1130	653
Syphilis	217	207	185
Trichinosis	0	0	0
Tuberculosis, pulmonary	189	124	197
Tuberculosis, other forms	6	8	14
Typhoid fever	0	0	1
Undulant fever	1	1	1
Whooping cough	51	200	217

Comment

Diseases below the seven-year median were diphtheria, bacillary dysentery, measles, mumps and whooping cough.

During March mumps was at the lowest level for this month since 1919.

During March whooping cough was at the lowest level for any month in the history of the State.

Diseases above the seven-year median were chicken pox, German measles, salmonellosis and scarlet fever.

Salmonellosis continues at a high level even though two other diseases that are spread via the enteric route — bacillary dysentery and infectious hepatitis — have declined from previously high levels.

Geographic Distribution of Certain Diseases

The following diseases were reported from the communities named:

Diphtheria: Arlington, 1; Boston, 2; total, 3.

Dysentery, bacillary: Greenfield, 1; West Bridgewater, 1; total, 2.

Encephalitis, infectious: Leominster, 1.

Hepatitis, infectious: Attleboro, 2; Bedford, 2; Belmont, 1; Boston, 6; Cambridge, 1; Fall River, 1; Framingham, 1; Hanson, 1; Haverhill, 2; Holyoke, 1; Hopkinton, 1; Lowell, 1; Malden, 3; Marshfield, 1; Millbury, 1; Natick, 1; New Bedford, 1; Rehoboth, 2; Shrewsbury, 1; Springfield, 1; Stoneham, 1; Taunton, 1; Waltham, 1; Wellesley, 1; Wilbraham, 1; total, 36.

Meningitis, meningococcal: Boston, 3; Holyoke, 1; Lynn, 1; Spencer, 1; Springfield, 1; Westport, 1; total, 8.

Meningitis, Pfeiffer bacillus: Holyoke, 1; North Reading, 1; Watertown, 1; total, 3.

Meningitis, pneumococcal: Arlington, 1; Lawrence, 1; Worcester, 1; total, 3.

Meningitis, undetermined: Cambridge, 1; Fall River, 1; Hamilton, 1; Ludlow, 1; Lynn, 2; Oxford, 1; Springfield, 1; Swampscott, 1; Westfield, 1; Weymouth, 1; Worcester, 1; total, 12.

Psittacosis: Amherst, 3.

Salmonellosis: Ashby, 1; Ashland, 1; Attleboro, 1; Boston, 9; Brockton, 1; Cambridge, 1; Chicopee, 1; Fitchburg, 1; Framingham, 1; Greenfield, 1; Haverhill, 2; Lynn, 2; Natick, 1; Newton, 1; Reading, 1; Salem, 1; Somerville, 4; Springfield, 2; Swampscott, 2; Wellesley, 1; Worcester, 1; total, 36.

CORRESPONDENCE

PLASMA ACETONE TEST

To the Editor: I read with great interest Dr. Alan S. Cohen's article on the differential diagnosis of salicylate intoxication and diabetic acidosis in the March 8 issue of the *Journal*. I think that the article is timely and gives necessary emphasis to a really difficult differential diagnosis. I should like to make one comment regarding this differential diagnosis that I do not believe was brought out completely by Dr. Cohen.

In the differential diagnosis of diabetic acidosis from other conditions involving diabetic patients I have found the plasma acetone test to be of great help. It has been my experience that in a patient with diabetic ketoacidosis with the degree of alkali deficit manifested by Dr. Cohen's patient, the plasma acetone test on a semiquantitative basis would surely be ++++ in at least the undiluted specimen and probably ++ or +++ in the 1:2 dilution. Although I have no personal experience with severe salicylate intoxication, I have had occasion to perform plasma acetone tests on patients taking 4 to 6 gm. (60 to 90 gr.) of aspirin daily for chronic rheumatoid arthritis. In these particular patients there were no detectable ketone bodies in the plasma. I grant that these patients did not manifest acute salicylism.

I am sure that patients with acute salicylate intoxication would show little, if any, acetonemia, as tested by the plasma acetone test. Those who see a fair number of cases of salicylate intoxication should utilize this test as an aid in the differential diagnosis. This would also establish experience with the test in acute salicylate intoxication. I personally believe that, for speed and simplicity, this test affords the best basis for the differential diagnosis of acute salicylate intoxication and diabetic acidosis.

Fred W. Whitehouse, M.D.

Detroit, Michigan

SUSPENSION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held March 1, 1956, it was voted to suspend the registration of Dr. Harben J. Boutourline-Young, Boston, Massachusetts.

Robert C. Cochrane, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

RESTORATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held March 15, 1956, it was voted to restore the registration of Dr. Jacob Norman, Dorchester, Massachusetts.

Robert C. Cochrane, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEW

Embryologie: Ein Lehrbuch auf allgemein biologischer Grundlage. By Prof. Dr. Dietrich Starck. 4°, cloth, 688 pp., with 502 illustrations. Stuttgart: Georg Thieme, 1955. DM 78.- $18.55. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

This interesting new book on embryology is subtitled "A Textbook of General Biologic Principles." Professor Starck achieves his objective of providing a broad biologic background, which he believes to be essential for the interpretation and understanding of vertebrate, especially mammalian, development. An impressive array of information from both descriptive and experimental embryology of invertebrates and vertebrates is drawn together in exposition of biologic principles. For an embryology text there is an unusually extensive treatment of genetics and of sex determination and differentiation. Considerable emphasis is placed on the embryology of mammals. Placentation is well presented from the phylogenetic point of view, with emphasis on higher primates. Unfortunately, the confusion of the human yolk sac with exocoelom is perpetuated in the text and illustrations.

Detailed information on fertilization and histogenesis is omitted. Yet, with his broad and comprehensive comparative anatomic approach, it was undoubtedly necessary for the author to limit some aspects of the subject. Also, with his approach, it is more difficult to follow through the development pattern of any one species than is possible in a more conventional study. This volume is well illustrated, containing many new and valuable original diagrams and photographs.

Among the textbooks written in the English language, there is probably no counterpart to this book. The usual type of textbook offered to the American student of medicine presents mammalian embryology in a restricted and isolated form. Certainly Professor Starck's broad comparative approach is a necessary prerequisite for an understanding of the intricacies of mammalian development, and phylogeny.

Helen A. Padykula, Ph.D.
George B. Wislocki, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Modern Medicine Annual 1956: An annual publication containing the articles that appeared in the twenty-four issues of Modern Medicine during 1955. Part Two. July 1 through December 15. 8°, cloth, 1025 pp., with illustrations. Minneapolis, Minnesota: Modern Medicine, 1956.

Tuberculosis in the Army of the United States in World War II: An epidemiological study with an evaluation of x-ray screening. By Esmond R. Long, M.D., director, Henry Phipps Institute, University of Pennsylvania; and Seymour Jablon, A.M., statistician, Follow-up Agency, Division of Medical Sciences, National Research Council, Washington, D.C. 8°, cloth, 88 pp., with 15 illustrations and 56 tables. Washington, D.C.: Superintendent of Documents, Government Printing Office, 1956. $1.50.

The Psychosomatic Genesis of Coronary Artery Disease. By Don Carlos Peete, M.D., associate clinical professor of medicine and lecturer in the history of medicine, University of Kansas School of Medicine. 8°, cloth, 220 pp., with illustrations. Springfield, Illinois: Charles C Thomas, 1955. $7.75.

Atlas of Plaster Cast Techniques. By E. E. Bleck, M.D., orthopedic surgeon, San Mateo Clinic, San Mateo, California; and Nellie Duckworth and Nancy Hunter, plaster and operating-room technicians, North Carolina Orthopedic Hospital, Gastonia, North Carolina. 8°, paper, 128 pp., with 347 illustrations. Chicago: The Year Book Publishers, Incorporated, 1956. $4.75.

The Laboratory Diagnosis of Cancer of the Cervix: Symposia on research advances applied to medical practice. No. 2. Edited by F. Homburger, M.D., research professor of medicine and director of the Cancer Research and Cancer Control Unit, Tufts University School of Medicine; and W. H. Fishman, Ph.D., research professor of biochemistry and nutrition and associate director of the Cancer Research and Cancer Control Unit, Tufts University School of Medicine. 8°, cloth, 72 pp., with 31 illustrations and 24 tables. New York: S. Karger, 1956.

Present Knowledge in Nutrition. Edited by Frederick J. Stare, Ph.D., M.D., professor of nutrition, Harvard Medical School and Harvard School of Public Health, and associate in medicine, Peter Bent Brigham Hospital, Boston. Second edition, revised and edited by the Editorial Staff and Advisory Board. 8°, paper, 130 pp. New York: The Nutrition Foundation, Incorporated, 1956. (Prepared from articles published in the journal, *Nutrition Reviews.*)

Who's Who in America: A biographical dictionary of notable living men and women. Vol. 29, 1956 and 1957. 4°, cloth, 3336 pp. Revised and reissued biennially. Chicago: The A. N. Marquis Company, 1956. $18.80. (Founded 1897 and published continuously since 1899 by Marquis-Who's Who, Incorporated, a nonprofit foundation.)

Epitome of the Pharmacopoeia of the United States and the National Formulary with Comments. Issued under the direction and supervision of the Council on Pharmacy and Chemistry of the American Medical Association. Tenth edition. 12°, cloth, 322 pp. Philadelphia: J. B. Lippincott Company, 1955. $3.00.

A Manual of Fractures and Dislocations. By Barbara Bartlett Stimson, M.D., Med.Sc.D., director, Department of Bone and Joint Surgery, St. Francis Hospital, Poughkeepsie, New York, chairman of trauma committee, Vassar Brothers Hospital, Poughkeepsie, and consultant in orthopedics, Hudson River State Hospital, Poughkeepsie, Sharon Hospital, Sharon, Connecticut, and Northern Dutchess Health Center, Rhinebeck, New York. Third edition. 12°, cloth, 224 pp., with 97 illustrations. Philadelphia: Lea and Febiger, 1956. $4.50.

The Year Book of Drug Therapy: 1955-1956 Year Book series. Edited by Harry Beckman, M.D., director, Department of Pharmacology, Marquette University Schools of Medicine and Dentistry, and consulting physician, Milwaukee County General and Columbia hospitals, Milwaukee, Wisconsin. 12°, cloth, 560 pp., with 64 illustrations and tables. Chicago: The Year Book Publishers, Incorporated, 1956. $6.00.

NOTICES

HENRY JACKSON LECTURE

The Henry Jackson Lecture, sponsored by the New England Cardiovascular Society, will be held in the Morse Auditorium, Museum of Science, Science Park, Boston, on Monday, May 14, at 8:15 p.m. Dr. Louis N. Katz will talk on the subject "The Role of Diet and Hormones in Atherosclerosis."

Interested physicians and medical students are invited.

NEW ENGLAND RHEUMATISM SOCIETY

The annual spring meeting of the New England Rheumatism Society will be held in the Stearns Auditorium, New England Medical Center, on Friday, May 18, at 8 p.m. The program is as follows:

Statistical Results of Sanatorium-Type Treatment in Rheumatoid Arthritis. Dr. Kurt Jellinek.

The Use of Ultrasound in Medicine. Dr. Thomas P. Anderson.

Rheumatoid Tenosynovitis. Drs. Robert Hormell, John G. Kuhns and Theodore Potter.

Proposed Diagnostic Criteria for Rheumatoid Arthritis. Dr. Marian W. Ropes.

AMERICAN NEUROLOGICAL ASSOCIATION

The eighty-first annual meeting of the American Neurological Association will be held at the Claridge Hotel, Atlantic City, New Jersey, June 18-20.

Further information may be obtained from Dr. Charles Rupp, Secretary, American Neurological Association, 133 South 36th Street, Philadelphia 4, Pennsylvania.

AMERICAN GASTROSCOPIC SOCIETY

The annual meeting of the American Gastroscopic Society will be held at the Knickerbocker Hotel, Chicago, on June 10 and 11.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The twenty-second annual meeting of the American College of Chest Physicians will be held at the Hotel Sherman, Chicago, June 6-10.

The scientific program will cover all aspects of heart and lung diseases. There will be a number of symposia, round-table luncheon discussions, seminars, motion pictures and a repetition of the "fireside conferences" inaugurated in 1955.

Examinations for fellowship in the College will be held on Thursday, June 7. Certificates of fellowship will be presented at the convocation before the Presidents' Banquet, on Saturday evening, June 9.

All physicians are invited to attend. Further information may be obtained from Executive Offices, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

THIRD NATIONAL CANCER CONFERENCE

The Third National Cancer Conference, sponsored jointly by the American Cancer Society and the National Cancer Institute of the United States Public Health Service, Department of Health, Education and Welfare, will be held in the Sheraton-Cadillac Hotel, Detroit, June 4-6.

A special feature during the Conference will be the public cancer forum on Tuesday evening, June 5.

Further information may be obtained from National Cancer Conferences Coordinator, American Cancer Society, 521 West 57th Street, New York 19, New York.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY

The seventeenth annual meeting of the Society for Investigative Dermatology will be held at the Hotel Sherman, Chicago, on June 9 and 10. In addition to the scientific session a cocktail party and dinner are planned.

Application for membership to the Society may be made up to the day before the meeting. Reservations for the cocktail party and dinner must be made before May 25. Further information may be obtained from Dr. Herman Beerman, Secretary-Treasurer, 255 S. 17th Street, Philadelphia 3, Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

May 3–5. American Association for Cleft Palate Rehabilitation. Page 774, issue of April 19.
May 3–5. American Goiter Association. Page 348, issue of August 25.
May 4 and 5. Sixth National Congress on Pediatrics. Page 491, issue of March 8.
May 4–29. Consultation Clinics for Crippled Children in Massachusetts. Page 819, issue of April 26.
May 8. Harvard Medical Society. Page 773, issue of April 19.
May 8. Cutter Lecture on Preventive Medicine. Page 824, issue of April 26.
May 9. Boston University School of Medicine. Alpha Omega Alpha. Page 824, issue of April 26.
May 14. Henry Jackson Lecture. Page 875.
May 14–17. Armed Forces Institute of Pathology. Page 774, issue of April 19.
May 14–18. American Nurses' Association. Page 491, issue of March 8.
May 15. South End Medical Club. Page 824, issue of April 26.
May 16–18. American College of Cardiology. Page 773, issue of April 19.
May 18. New England Rheumatism Society. Page 875.
May 22–24. Massachusetts Medical Society Annual Meeting. Page 868.
May 23. Boston Branch, American Medical Women's Association. Page 773, issue of April 19.
May 28–June 1. European Symposium on Vitamin B. Page 578, issue of September 29.
June 1–9. International Medical-Surgical Meetings. Page 540, issue of March 15.
June 4–6. Third National Cancer Conference. Notice above.
June 4–13. Army Medical Service Postgraduate Course. Page 84, issue of July 14.
June 6–10. American College of Chest Physicians. Notice above.
June 9 and 10. Society for Investigative Dermatology. Notice above.
June 10 and 11. American Gastroscopic Society. Page 875.
June 18–20. American Neurological Association. Page 875.
June 21–23. Society of Nuclear Medicine. Page 1092, issue of December 15.
June 21–24. American Academy of Dental Medicine. Pag 994, issue of December 1.
August 19–23. American College of Chest Physicians. Page 840, issue of November 10.
September 3–5. Congress on Blood Transfusion, Blood Banks and Hematology. Page 297, issue of February 9.
September 10–14. American Dietetic Association. Page 1180, issue of December 29.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, MAY 10

THURSDAY, MAY 10

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Guest Speaker of the Bingham Associates. Management of Patient with Jaundice. Dr. Fernando A. Rubio. Cape Cod Hospital, Hyannis, Massachusetts.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Staff Conference. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Tumor Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.
*3:00 p.m. Thoracic Conference. Surgical Management of Angina Pectoris. Drs. Laurence B. Ellis and Dwight E. Harken. Main Amphitheater, Peter Bent Brigham Hospital.
5:00 p.m. Case Presentation and Pathological Discussion Followed by a Subject of Special Presentation. Joslin Auditorium, New England Deaconess Hospital.

FRIDAY, MAY 11

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. Thorndike Amphitheater, Boston City Hospital.
*1:00–3:00 p.m. Combined Medical-Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–6:00 p.m. X-Ray Conference. Dr. Merrill Sosman. Pratt Auditorium, New England Center Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, MAY 12

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:30–11:00 a.m. Surgical House Officers' Conference. Second-Floor Conference Room, Carney Hospital, Dorchester.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference (Blood Clinic). Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, MAY 14

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.

(Concluded on page xxii)